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FORCED GRASPING AND GROPING IN RELATION TO THE SYNDROME OF THE PREMOTOR AREA

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Recent experimental studies [1] have indicated that forced grasping is an exaggerated postural reflex which may be induced in all animals of the primate series by lesions restricted to the premotor area of the cerebral cortex. The grasping phenomenon, however, is not an isolated reflex disturbance, since it is always associated with a number of equally striking signs and symptoms which taken together form, both in man and in animals, a well defined entity in neurology. This entity has been variously designated as "tonic innervation" [2] and as the "syndrome of the premotor area." [3] As the physiologic basis of the syndrome is not yet clearly understood, the present experimental study was undertaken, in which special attention has been given to forced grasping and groping.

METHODS

Monkeys, baboons and chimpanzees were used as experimental subjects. Prior to operation many of the animals were trained to perform complex skilled movements, e. g., to open problem boxes requiring grasping, rotation of levers, moving of cranks, etc., as described by Jacobsen.[4] All operative procedures were carried

Read at the meeting of the New York Neurological Society, Dec. 5, 1933.

From the Laboratory of Physiology, Yale University School of Medicine.

1. (*a*) Richter, C. P., and Hines, Marion: Experimental Production of the Grasp Reflex in Adult Monkeys by Lesions of the Frontal Lobes, Research Publication, Association for Research in Nervous and Mental Diseases, 1932, to be published; preliminary communication, Am. J. Physiol. **101**:87, 1932. (*b*) Fulton, J. F.; Jacobsen, C. F., and Kennard, M. A.: A Note Concerning the Relation of the Frontal Lobes to Posture and Forced Grasping in Monkeys, Brain **55**:524, 1932. (*c*) Bieber, I., and Fulton, J. F.: The Relation of Forced Grasping and Groping to the Righting Reflexes, to be published; preliminary communication, Am. J. Physiol. **105**:7, 1933.

2. Wilson, S. A. K., and Walshe, F. M. R.: The Phenomenon of "Tonic Innervation" and Its Relation to Motor Apraxia, Brain **37**:199, 1914.

3. Kennard, M. A.; Viets, H. R., and Fulton, J. F.: The Syndrome of the Premotor Cortex in Man: Impairment of Skilled Movements, Forced Grasping, Spasticity, and Vasomotor Disturbance, Brain, to be published.

4. Jacobsen, C. F.: A Study of Cerebral Function in Learning: The Frontal Lobes, J. Comp. Neurol. **52**:271, 1931; The Influence of Extirpation of the Frontal Lobes and of the Motor Area upon the Retention of Acquired Skilled Movements in Monkeys and Chimpanzees, Research Publication, Association for Research in Nervous and Mental Diseases, 1932, to be published.

out by modern neurosurgical methods previously described from this laboratory.[5] Extirpations of the cortex were generally made with a Davis-Bovie knife, and records of the lesions and of the chief anatomic landmarks on the surface of the cortex were made by tracing them on cellophane at the time of operation. Both ether and sodium amytal were used as anesthetics, ether being employed when the excitability of the premotor area was under study. The excitability of the cortex was explored by means of monopolar faradic stimulation with the diffuse electrode placed in the rectum. The cyto-architecture of all blocks of tissue removed was examined in histologic sections; after the death of the animal, the lesions themselves, together with the degeneration incident to them, were similarly studied (by the Marchi or by the Weigert-Pal method).

FORCED GRASPING AS SEEN IN ANIMALS

The discovery of Richter and Hines,[1a] announced in 1932, that isolated lesions of the premotor area of monkeys (area 6 of Brodmann) cause reflex grasping in the opposite extremities opened a new and fruitful chapter in modern neurophysiology. Richter and Hines pointed out that lesions restricted to the cortex may give rise to this phenomenon and that the response is specific for the premotor area, since extirpations elsewhere in the hemispheres failed to cause it. They measured the intensity of the grasping quantitatively by determining the length of time that an animal would remain suspended from an iron bar placed in the palm of an affected extremity. The grasp was present in its full intensity immediately after a unilateral lesion of the premotor area, but it gradually disappeared within a week or ten days. It appeared in both upper extremities when the premotor area of the opposite hemisphere was removed, but again waned on both sides after two or three weeks. Richter and Hines did not discuss the relation of grasping to groping or to the other manifestations of the premotor syndrome.

A Preparation Showing Permanent Grasping.—In order further to analyze the underlying mechanism of grasping, it was essential to obtain a preparation in which the phenomenon was present over a period of weeks or months. It is significant that such a state of permanent grasping has been produced only in animals that have suffered complete paralysis of movements of cortical origin—movements which are generally referred to somewhat loosely as "volitional" or "voluntary."

In seeking to produce permanent grasping a series of experiments was carried out in collaboration with Kennard in which the motor and premotor areas, first of one hemisphere and then of the other, were removed seriatim.[6] Sometimes the

5. Fulton, J. F., and Keller, A. K.: The Sign of Babinski, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

6. (*a*) Fulton, J. F., and Kennard, M. A.: A Study of Flaccid and Spastic Paralyses Produced by Lesions of the Cerebral Cortex in Primates, Research Publication, Association for Research in Nervous and Mental Diseases, 1932, to be published; (*b*) The Localizing Significance of Spasticity, Reflex Grasping, and the Signs of Babinski and Rossolimo, Brain **56**:213, 1933. (*c*) Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318, 1933.

motor area was removed first, and sometimes the premotor area (fig. 1), four successive operations generally being performed. It was found that if a small part of either the motor or the premotor area of one hemisphere remained intact, even though both areas were completely destroyed in the opposite hemisphere, the animal regained a certain measure of power in all four extremities (feeding, running and climbing movements), but forced grasping was not permanently demonstrable. When the remaining area was destroyed, the animal lapsed at once into a state of complete and permanent cortical paralysis affecting all four extremities, and forced grasping was thereafter permanent.

There is at present in this laboratory a baboon from which the motor and premotor areas have been entirely removed on one side, and in which a small part of the premotor area and of the motor arm area of the opposite side still remains. The animal has continued in this condition for a year and a half, competing suc-

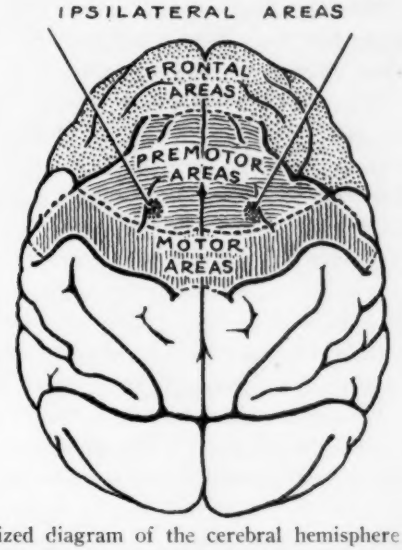

Fig. 1.—A life-sized diagram of the cerebral hemisphere of a rhesus monkey (Macaca mulatta), showing the principal areas of the frontal lobes. The motor area begins at the base of the central sulcus and extends rostrally to the premotor area, in which region the Betz cells disappear; the premotor area extends to the arcuate sulcus rostrally and to the sulcus cinguli mesially; the frontal area comprises the region of the cortex rostral to the arcuate sulcus. The ipsilateral areas, described by Bucy and Fulton,[6c] lie mesially to the superior precentral sulci and within the premotor areas.

cessfully with its fellows. The animal is stiff on the side opposite the complete extirpation, but it is nevertheless able to feed itself and to run, climb and carry out cortically integrated movements in all four extremities. On the basis of previous experience, we can predict that when the remaining area is destroyed the animal will never again move its extremities—"voluntarily"—and forced grasping will be as permanent as the cortical paralysis.

The motor and premotor areas are known as areas 4 and 6 in Brodmann's[7] well known architectonic map. For convenience, animals with the motor and

7. Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, ed. 2, Leipzig, Johann Ambrosius Barth, 1925.

premotor areas removed from both hemispheres will be referred to as "bilateral area 4 and 6 preparations."

Grasping and the Pyramidal Tract.—It is generally stated in the clinical literature [8] that grasping resulting from an expanding lesion of the frontal lobe disappears when the tumor involves the pyramidal tracts. It may seem paradoxical, therefore, that grasping is seen permanently only in animals in which the pyramidal tract has been completely destroyed. This paradox is probably to be explained as follows: In chimpanzees, which neurologically are nearer human beings than monkeys are, forced grasping is generally well developed for from ten days to two weeks after a lesion restricted to the premotor area. It is associated incidentally with spasticity of the extremities and with marked increase of the tendon reflexes. If the adjacent motor area is removed from such an animal during the period in which forced grasping is present, the opposite extremities lapse into a state of profound flaccid paralysis with absence of tendon reflexes and disappearance of forced grasping. In the course of five or six days, however, the tendon reflexes return, the extremities again become spastic, and soon afterward forced grasping once more appears; well developed grasping is never present, however, until appropriate lesions have been made in the opposite hemisphere. In man, one is not likely to see forced grasping in association with a pyramidal lesion, since the depression of reflexes resulting from destruction of the pyramidal tract is undoubtedly greater in the acute phase, e. g., after a capsular hemiplegia, than it is in the chimpanzee, and the stage of reflex recovery from the pyramidal lesion probably comes after a greater interval than that required for pure premotor forced grasping to disappear spontaneously.

SEPARATION OF GRASPING FROM GROPING

Before proceeding to a more intimate analysis of the phenomenon of grasping, it is essential to define certain terms. Forced grasping refers to the reflex flexion response of the digits of either the hands or the feet, generally induced by gentle contact with certain restricted areas of the palmar or plantar skin. Human beings exhibiting such a response experience difficulty in releasing the grasp. Walshe and Robertson [9] pointed out, in their stimulating discussion of "grasping movements," that in human beings with the premotor syndrome (which

8. (*a*) Adie, W. J., and Critchley, M.: Forced Grasping and Groping, Brain **50**:142, 1927. (*b*) Schuster, P., and Pinéas, H.: Weitere Beobachtungen über Zwangsgreifen und Nachgreifen und deren Beziehungen zu ähnlichen Bewegungsstörungen, Deutsche Ztschr. f. Nervenh. **91**:16, 1926.

9. Walshe, F. M. R., and Robertson, E. Graeme: Observations upon the Form and Nature of the "Grasping" Movements and "Tonic Innervation" Seen in Certain Cases of Lesions of the Frontal Lobe, Brain **56**:40, 1933.

they termed "tonic innervation") the grasping movements are generally more complicated than the grasping reflexes just described as present in paralyzed monkeys. They emphasized that normally there is a "volitional," i. e., a cortical, component in the grasp, arising from visual stimuli, and sometimes in that arising from tactile stimuli. They argued, therefore, that the term "forced grasping" as applied to the clinical phenomenon is a misnomer, since it implies a purely "reflex" response, and they suggested that this form of grasping, in which the cortex participates, should be referred to as an "automatic" movement. They recognized that a second component of the grasp is not under cortical control and that the appropriate stimulus for the noncortical phase is stretching of the flexor tendons. The point is well taken, but one detects a serious fallacy in their logic. Modern neurophysiology has only one fundamental tenet in its creed, namely, that all movements, whether they involve the cortex or merely the lower reflex centers, are ultimately reflex. No more excellent example of a highly integrated reflex can be imagined than Walshe's "automatic" groping and grasping in response to a visual stimulus—clearly a more highly organized reaction than the grasp of a paralyzed animal.

After this preamble, the relevant terms can be somewhat more closely defined:

Definitions.—Forced grasping includes the complex grasping reactions demonstrable in primates (including man) with lesions of the premotor area; the basic reflex is noncortical but is subject to cortical modification from visual, tactile and proprioceptive sensory channels. The adjective "forced" is clearly a happy one, since it implies "compulsion" and "automatism" with restriction, but not absence, of cortical control.

Groping, a phenomenon seen under the same conditions, refers to the sequence of rhythmic reaching movements of an extremity preparatory to the grasp. Unlike the grasp itself, groping is a cortical reflex arising chiefly from visual stimuli. It disappears when the pyramidal tract is destroyed, and it generally ceases when vision is abolished. It is thus clearly an "automatic" or a "compulsive" movement integrated at the cortical level.

Groping which depends on visual stimuli should be carefully distinguished from a somewhat similar rhythmic movement, known as *rhythmic righting reactions,* seen in cortically paralyzed primates and in thalamic animals when the position of the body is changed in space. These rhythmic righting movements come from the labyrinth and the body proprioceptors, rather than from the visual pathways through the cortex.

Finally, the *grasp reflex,* the basis of forced grasping, is a complex postural response involving chiefly the digital flexors and is integrated

entirely subcortically. It is invariably present in monkeys and chimpanzees from which the motor and premotor areas have been removed bilaterally, and its characteristics are unaltered when both hemispheres are removed and the animal is thus made into a thalamic preparation. An analysis of the grasp will be taken up in the next section, and groping will now be considered in somewhat greater detail.

Groping.—Groping is a phenomenon that occurs after certain lesions of the frontal lobe in response to a moving object passing within the field of vision. That it depends on the integrity of a part of the cortex has been clearly shown in monkeys. It has been seen in animals in which the frontal and premotor areas on both sides have been removed (fig. 2), and it does not appear to be well developed in animals with lesions restricted to a premotor area. The reaction is generally slow and delib-

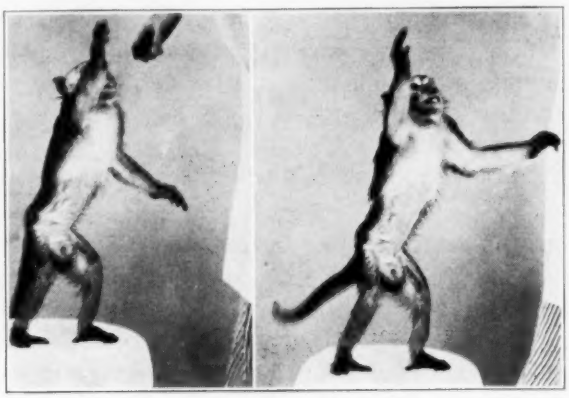

Fig. 2.—Two photographs showing groping in a Java monkey (Macaca irus) from which the frontal and premotor areas had been removed three weeks previously. The stimulus was the observer's finger moving within the animal's field of vision.

erate, is peculiarly automatic and can be made to occur time after time in monotonous repetition. In the Java monkey shown in figure 2, in which the frontal and premotor areas on both sides had been extirpated, the groping movements on the eighth day after bilateral extirpation were described as follows:[10]

> After the first week, when any object was brought within a radius of 1 to 2 ft. in its field of vision the animal would grasp it slowly but firmly after a latency of ten to thirty seconds; once grasped the object would be held for minutes at a time without change of attitude. Sometimes when the object was held just out of its reach the animal would direct its hand toward it and the posture so induced would be retained, as if "frozen" in that position for minutes at a time.

10. Fulton, Jacobsen and Kennard,[1b] p. 529.

All purposeful movements were notably slow in starting during the first three weeks and always continued after their usefulness was over. Thus, when the hand was brought to the face with food it stayed there and often clutched the food while the animal was at the same time trying to consume it. Once a movement, such as walking or chewing, was initiated, the animal would continue the movement for an unlimited time, to the exclusion of all other activity and in complete disregard of external stimuli which would readily divert a normal monkey.

The same phenomenon has since been seen in other monkeys in which the lesions were made seriatim instead of simultaneously as in the instance just cited. The movements are always deliberate, and, as the foregoing quotation indicates, the animals exhibit perseveration. Thus, any movement depending on cortical levels of integration tends to continue beyond its allotted time. If the animal extends its hand for food, the extremity is likely to remain extended for twenty seconds or more; if it walks to the edge of the table, it sometimes remains there for as long as two minutes in a curious frozen posture before determining to make a leap. If given a piece of sugar, the animal continues to crunch at it rhythmically long after the sugar is completely dissolved. The phenomenon of groping and the perseveration of groping movements are clearly cortical, as they disappear completely when the pyramidal tracts are removed; moreover, groping does not occur except when objects are brought into the field of vision, indicating that the reaction depends chiefly, if not entirely, on visual stimuli.

Grasping and Groping and the Corpus Callosum.—Schuster and Caspar [11] and Schuster and Pinéas [8b] have reported the occurrence of forced grasping and groping in cases of large tumors of the corpus callosum. In view of this and of the fact that the frontal lobes are richly interconnected through the corpus callosum, it might be thought that transection of the corpus would produce or alter the grasp. Armitage and Meagher [12] in their painstaking study of tumors of the corpus callosum, reported a series of observations on experimental transection of this body in monkeys. The transections were made before and after removal of the arm areas. These observers were unable to find any increase of hemiplegic symptoms in motor area preparations as a result of section of the corpus callosum, and they did not detect grasping or groping. Kennard and Watts [13] similarly did not find that grasping or groping

11. Schuster, P., and Caspar, J.: Zwangsgreifen und Stirnhirn (sowie einige Bemerkungen über das occipito-frontale Bündel), Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:739, 1930.

12. Armitage, G., and Meagher, R.: Gliomas of the Corpus Callosum, Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:454, 1933.

13. Kennard, M. A., and Watts, J. W.: The Effect of Section of the Corpus Callosum on the Motor Performance of Monkeys, J. Nerv. & Ment. Dis., to be published.

was produced by primary transection of the corpus callosum in monkeys, nor did they find grasping augmented by this operation in premotor preparations.

It remains, therefore, to consider the reflex mechanism of the grasp reflex itself.

THE NONCORTICAL COMPONENTS OF FORCED GRASPING (THE THALMIC GRASP)

In a study of the relation of forced grasping to the postural reflexes carried out in collaboration with Dr. Irving Bieber,[1c] it was found, as already mentioned, that the grasp was permanent in bilateral motor and premotor preparations (monkeys and baboons). In making extirpations for this study the motor face area was left intact, since this greatly facilitated feeding and nursing. When a lump of sugar was brought into the field of vision of such a preparation, violent chewing movements occurred, and the animal licked its lips with its tongue and sometimes attempted to elevate its head. The extremities did not move, except for occasional alterations in posture incident to voluntary movement of the neck muscles, and there was no groping. When the sugar was placed in the animal's hand, a vigorous grasp reflex came on, but the animal could not bring the sugar to its mouth; vigorous attempts were made, however, through the cortical innervation of the neck muscles, to bring the head to the lump of sugar. The grasping of the lump of sugar might continue for hours.

The Grasp, a Subcortical Reflex.—That the grasp itself is independent of the cortex is evident, since it also occurs unchanged in a completely decorticated monkey; moreover, the alterations in the intensity of the grasp with change of position of the body in space are identical in decorticate and in bilateral area 4 and 6 preparations. When the thalamic area is excluded by transection of the brain stem in the hypothalamic area, grasping disappears. Further studies are needed to determine the exact level at which the disappearance occurs.

The Grasp and the Righting Reflexes.—The postural pattern of a thalamic monkey changes with the position of the body in space, and these alterations, which were fully described by Magnus,[14] are identical with those seen in bilateral area 4 and 6 preparations. When the animal lies in the lateral position, there is pronounced extension of the underlying limbs, with flexion of the limbs on the upside. When the animal is turned over, the pattern of response is reversed. It is highly significant that when the animal is in the lateral position the grasp is well

14. Magnus, R.: Körperstellung und Labyrinthreflexe beim Affen, Arch. f. d. ges. Physiol. **194**:396, 1922.

marked only in the extremities on the upside; thus, if the animal is on its right side, the left hand (and the left foot) exhibit a vigorous grasp reflex, as shown in figure 3. The right extremities show little or no grasping, provided the animal's head is reclining quietly on the table. The changes in the pattern of postural response fall into the category of body-righting reflexes. Magnus [14] showed that these changes persist in thalamic preparations after the labyrinth has been destroyed; the postural response, moreover, may be inhibited when the animal is in the lateral position by applying uniform pressure to the upside of the body. Though my associates and I have not yet studied the influence of the labyrinth on the grasp, Dr. Bieber [1c] was also able to show in area 4 and 6 preparations that uniform pressure applied to the upside of the body

Fig. 3.—A monkey (Macaca mulatta) with the motor and premotor areas removed from both hemispheres lying on the right side. A strong grasp reflex is present in the left (the uppermost) hand, but not in the right. Note also the extended position of the right upper extremity.

inhibited the grasp and made the posture of the extremities symmetrical on the two sides.

When such a preparation is turned over rapidly the extremities may exhibit rhythmic movements similar to those shown by a dog or a cat attempting to right itself from the lateral position. In the case of a monkey these rhythmic movements may continue until the hand encounters a solid graspable object, when the rhythmic movements immediately cease and the body, through the grasp, tends to be pulled into the horizontal position. From these observations, particularly from the fact that the grasp follows other body-righting reflexes, we have concluded that the grasp is part of the righting reflex mechanism peculiar to primates. In the presence of the cortex the grasp subserves other more highly integrated functions, but in the absence of the cortex the grasp reverts to the primitive group of postural reactions from which it took origin.

In unilateral preparations the grasp also changes in intensity with the position of the body. Thus, if the premotor area has been removed from one hemisphere of a chimpanzee the grasp may be present in nearly all positions for the first four or five days, being minimal when the animal lies on the side opposite the cortical lesion. If it becomes difficult to demonstrate the grasp when the animal is in the upright position, the reaction can be brought out by causing the animal to lie in the lateral position with the affected side up. This, incidentally, is the position in which forced grasping is most likely to be demonstrated in clinical cases.[3]

Sensory Components of the Grasp.—Since visual pathways and other cortical mechanisms have been excluded as essential to the grasp, the relative importance of the cutaneous and the proprioceptive sensory channels may now be considered.

Cutaneous Receptors: In thalamic monkeys and in human beings exhibiting forced grasping the grasp may be evoked by very gentle contact with the palmar skin, especially over the metacarpophalangeal joints. Some subjects are so sensitive that deep sensibility would seem to be excluded as being in any way involved in initiation of the response. A gentle stroke with a camel's hair brush was said to be an adequate stimulus in one case, but this degree of sensitivity has not been seen in monkeys. More often, fairly firm contact is necessary, and in monkeys, when the response is waning after a unilateral lesion, tension must be applied to the flexor tendons before the response appears. Clearly, a purely cutaneous stimulus is adequate in some instances to initiate the grasp, but it can be shown readily in animals that it is not essential for the response.

The skin of the hand of a bilateral 4 and 6 macaque was completely anesthetized by the injection of procaine hydrochloride around the wrist and into the palmar skin (Bieber and Fulton[1c]). When the animal ceased to react to pinpricks and to vigorous pinching of the skin of the digits, the grasp could still be evoked in marked form by applying slight pressure to the palm or to the fingers in such a way as to stretch the flexor tendons slightly. Though more difficult to evoke than before the procaine hydrochloride had been given, the grasp developed normally and was of sufficient intensity to maintain the weight of the body. We concluded from this observation that, although the skin receptors were not essential to the reaction, they undoubtedly contributed to it and that in a sensitive preparation they may initiate the response. In this respect the interaction between the cutaneous sense organs and the proprioceptive end-organs is similar to that demonstrated by Magnus[15] for the positive supporting reaction.

15. Magnus, R.: Körperstellung: Experimentell-physiologische Untersuchungen über die Einzelnen bei der Körperstellung in tätigkeit tretenden Reflexe, über ihr Zusammenwirkung und ihre Störungen, Berlin, Julius Springer, 1924.

Deep or Proprioceptive Receptors: Human beings exhibiting forced grasping generally show exquisitely sensitive tendon reflexes of the digits, as exemplified by the signs of Hoffmann and Rossolimo. Walshe and Robertson [9] even insisted that the noncortical component of forced grasping is entirely proprioceptive in origin. For reasons stated in the preceding paragraph, we cannot accept this conclusion, but we heartily support these authors in emphasizing the importance of stretching of the tendons as a stimulus for the elicitation of the grasp.

The part played by the deep receptors has been studied experimentally by section of posterior nerve roots. In a series of monkeys that I studied in collaboration with Bieber [1c] and in animals studied by Kennard,[16] posterior nerve roots supplying the upper extremity were severed in bilateral area 4 and 6 preparations and in normal monkeys which later had the appropriate areas of the cortex removed. The results, which will later be published in detail, may be summarized as follows:

1. Section of posterior nerve roots from the fourth to the eighth cervical segment diminishes the grasp slightly, but if the affected extremity is manipulated so as to produce slight extension of the shoulder muscles (innervated by the thoracic segments), the grasp occurs vigorously.

2. Section of posterior nerve roots from the first cervical to the eighth thoracic segment abolishes the grasp induced by stretching the muscles of the shoulder.

3. However, a sudden change of the position of bilateral area 4 and 6 preparation may cause the grasp to appear in the completely deafferented extremity. The conditions essential for its appearance are now under observation. Apparently the postural reflex pattern of a thalamic preparation can manifest itself in a completely deafferented preparation, just as decerebrate rigidity may appear in the deafferented upper extremities of the cat and the dog when induced by labyrinthine stimuli (Pollock and Davis [17]).

From these observations it is clear that the grasp is a fundamental part of the neurologic organization of the animal, since it can manifest itself in complete absence of the sensory innervation of the affected extremity.

Proprioceptive Labyrinthine Components: If the grasp still occurs after the entire afferent supply of the extremity has been destroyed, it is obvious that some other source of sensory innervation must be considered. In one experiment the hind limbs and the body pro-

16. Kennard, M. A.: Unpublished studies.

17. Pollock, L. J., and Davis, L.: Studies in Decerebration: VI. The Effect of Deafferentation upon Decerebrate Rigidity, Am. J. Physiol. **98**:47, 1931.

prioceptors were excluded by section of the cord without altering the grasp. The sources of afferent stimulation require further study, as does the labyrinth, which is probably the chief sensory source of these reaction patterns.

FORCED GRASPING IN THE PREMOTOR SYNDROME

Wilson and Walshe [2] were the first to emphasize that cases of grasping showed other abnormal manifestations, which they grouped together under the term "tonic innervation." The disadvantages of using the term "tonic" are now obvious, and it seems preferable to describe the disturbance in terms of the individual reflex mechanisms which become altered. The syndrome of the premotor area seen both in man and in animals is characterized by four outstanding manifestations.

1. *Impairment of Skilled Movements.*—Appearing first in clinical cases and persisting longest in experimental animals, disturbance of acquired skilled movements may be looked on as the primary symptom of isolated lesions of the premotor area. This is not a new conception, for the premotor region has been regarded since the time of Campbell,[18] in 1905, as the part of the brain in which, as happily stated by Tilney and Riley,[19] "motion formulae for skilled acts are constructed and retained." This statement of the functions of the premotor area coincides entirely with experimental evidence concerning its activities. Animals trained to perform skilled movements suffer impairment of the capacity to execute delicately adjusted maneuvers after the premotor area has been destroyed. The extent of the deficit diminishes with time, but a residual can always be readily detected, especially in chimpanzees. Gross power is not, however, impaired, and in human beings the grip may be good even when awkwardness and difficulty exist with regard to other forms of voluntary activity.

2. *Spasticity and Increase of Reflexes.*[6b]—Appearing early in human beings with premotor lesions and persisting indefinitely in experimental animals, spasticity and the associated increase of tendon reflexes must also be regarded as a distinctive manifestation of a premotor lesion. Motor lesions, on the other hand, especially if acute, give rise to depression of reflexes and generally to flaccid paralysis. This is invariably true in experimental animals, and it also appears to be the case clinically when the lesions are restricted to the motor area. The degree of spasticity alters with the subject's position in space, indicating that the

18. Campbell, A. W.: Histological Studies on the Localization of Cerebral Function, London, Cambridge University Press, 1905.

19. Tilney, F., and Riley, H. A.: The Form and Functions of the Central Nervous System; An Introduction to the Study of Nervous Diseases, New York, Paul B. Hoeber, Inc., 1923.

spastic phenomena are probably manifestations of the righting reflex mechanism. It has long been known, for example, that in hemiplegia in man a change from the erect to the supine position increases the flexor posture of the upper extremities, and that in the lateral position flexor posture is maximal. This, as has recently been shown in a clinical case,[3] is also true of spasticity arising from lesions restricted to the premotor area.

The superficial reflexes, such as the Babinski reflex, are somewhat altered by changes in position in space, but they have not yet been adequately studied from this point of view.

3. *Forced Grasping.*—Appearing late in clinical cases, forced grasping is an integral part of a fully developed premotor syndrome; and it is undoubtedly significant that, though it appears late clinically, it disappears early following experimental lesions. The basic reflex pattern essential for the appearance of forced grasping is fully uncovered only when all the motor projection systems of the motor cortex are destroyed. Forced grasping as it appears clinically is a complex phenomenon with cortical components involving the visual pathways and subcortical components involving nuclei at the thalamic level; and, like spasticity, it is fundamentally a manifestation of the postural and the righting reflex mechanism.

4. *Vasomotor Changes.*[20]—A symptom which has been too little studied in clinical cases is the vasomotor disturbance invariably seen at some stage following a premotor lesion, generally late. In an experimental animal, the destruction of the premotor area causes increased sweating on the opposite side for a week or ten days; in a warm, dry atmosphere this causes marked lowering of the temperature of the affected extremity. Some patients tend to show a predominance of vasomotor effects, i. e., dilatation of minute vessels and edema, and others, a predominance of sudorific effects, i. e., increased sweating and fall of temperature. Whether these different manifestations are of localizing value remains to be determined, but the existence in the cortex of a region controlling vasomotor responses should be emphasized, and the area deserves to be more widely studied. Following faradic stimulation of the premotor area, changes in gastro-intestinal activity have also been observed;[21] moreover, after bilateral premotor area lesions four of our animals died of acute intussusception with obstruction. The significance of this finding has been discussed by

20. Kennard, M. A.: Vasomotor Representation in the Cerebral Cortex, Science, to be published. Kennard, Viets and Fulton.[3]

21. Watts, J. W., and Fulton, J. F.: Intussusception—the Relation of the Cerebral Cortex to Intestinal Motility in the Monkey, Surg., Gynec. & Obst., to be published.

Watts and Fulton;[21] in conjunction with the vasomotor phenomena just described, it indicates clearly that the premotor cortex possesses rich autonomic representation.

SUMMARY AND CONCLUSIONS

The grasping reflexes of monkeys and chimpanzees have been studied in order to elucidate the physiologic basis of the phenomenon of forced grasping in man. These prehension responses include a number of individual reactions which may be defined as follows: 1. Forced grasping is a reaction exhibited by primates with lesions of the premotor area of the cortex. It is a highly complex response which is subject to modification by visual and tactile integrations at the cortical level. 2. Groping, a compulsive reaching movement preparatory to the grasp, is seen only when grasping is marked. It arises primarily from visual stimuli, is integrated at the cortical level and is generally confined to the upper extremity. 3. The grasp reflex, the basis of forced grasping, is a purely subcortical reaction, which forms a part of the righting reflex mechanism of primates. 4. Rhythmic righting movements are a complex group of reactions, prodromal to the grasp, present in thalamic monkeys. These movements, which affect all extremities, occur whenever the position of the body is rapidly changed in space, and they undoubtedly arise in part from labyrinthine stimulation.

The observations made in this study and the conclusions drawn therefrom are as follows:

1. When the motor and the premotor area are removed from both hemispheres of monkeys or baboons (bilateral area 4 and 6 preparations), the animals suffer complete and permanent paralysis of all cortically integrated movements, and the postural reflexes of such animals are identical with those of completely decorticated monkeys.

2. The grasp reflex is permanently present in bilateral area 4 and 6 preparations.

3. The grasp reflex changes in intensity with the position of the body in space, thus falling into the category of body-righting reflexes. It is also subject to modification from the labyrinth.

4. The grasp reflex of bilateral area 4 and 6 preparations is still present: (1) after the skin of the palm has been anesthetized; (2) after the posterior nerve roots from the third to the eighth cervical segment have been severed, when stretch is applied to the shoulder muscles, thoracically innervated, and (3) after section of all posterior roots from the third cervical to the eighth thoracic segment, when the position of the body is changed in space. The grasp reflex is therefore a fundamental part of the postural and the righting reflex mechanism, and as a pattern of response it is independent of the sensory innervation of the extremity.

5. Forced grasping in man and in animals is also subject to variations of intensity with changes of position of the body in space, being maximal when the body is in the lateral position with the affected extremity uppermost.

6. Forced grasping is an integral part of the clinical syndrome of the premotor area. This syndrome is characterized by: (1) impairment of skilled movements without gross loss of motor power; (2) spasticity and increase of tendon reflexes; (3) forced grasping, and (4) vasomotor disturbances in the affected extremity.

LEAD AS A POSSIBLE CAUSE OF MULTIPLE SCLEROSIS

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In a report on lead poisoning published in 1925, Aub, Fairhall, Minot and Reznikoff [1] drew the following conclusions: Most of the lead absorbed into the body is deposited in the skeleton, where its behavior resembles calcium in many respects. Stored lead is apparently harmless, but the skeletal deposits may be released by a slight change toward either the acid or the alkaline side of the usual hydrogen ion concentration of the organism. They proved that abnormalities of diet or certain pathologic conditions bring about such changes and so release the rather unstable deposits of lead, flooding the organism with soluble lead. The mechanism of acute toxic attacks which occur in lead poisoning as a result of infections or of acidosis is at once apparent.

This study of lead in relation to multiple sclerosis was inaugurated in November, 1932, by the discovery made by one of us (W. C.) that the cerebrospinal fluid of a patient suffering from multiple sclerosis contained lead (case 2). The search for lead in this case had been previously suggested by the study of a frank case of lead poisoning which came to autopsy from the Presbyterian Hospital, New York, in 1925. In this case the technic that had just been described by Aub, Fairhall, Minot and Reznikoff [1] was employed.

Our attention was first called to lead as a possible cause of multiple sclerosis by the case of a patient initially presenting himself with typical signs of retrobulbar neuritis. The signs had developed following a

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Prof. J. C. Meakins, of the Department of Medicine, placed the facilities of the medical laboratories at our disposal and permitted us to use ward beds in his service, in addition to providing much helpful criticism and encouragement. Miss Doris Brophy, B.Sc., carried out detailed and exacting analyses in an efficient manner.

1. Aub, J. C.; Fairhall, L. T.; Minot, A. S., and Reznikoff, Paul: Lead Poisoning, Medicine **4**:1, 1925.

severe infection of the throat. Lead was demonstrated in the stools and urine. When attempts were made to promote its excretion, ascending myelitis developed, and then lead was demonstrated in the cerebrospinal fluid by Fairhall's hexanitrite method.[2] The administration of calcium stopped the advance of signs, caused lead to disappear from the spinal fluid, and reduced the amounts found in the excreta. With continued administration of calcium no further advance took place in spite of the fact that urinary sepsis and infected bed sores developed and eventually caused death. Lead was demonstrated in the bones, liver, brain and spinal cord. The demyelinization in the spinal cord was much more extensive than that occurring in typical multiple sclerosis, and secondary degenerations took place. In the brain and cerebellum, however, typical sclerotic plaques were present.

CASE 1.—*History.*—H. S., a colored man, aged 36, was admitted to Dr. W. Penfield's neurosurgical service at the Presbyterian Hospital, New York, on Dec. 29, 1925, complaining that for three days he had been completely blind. He had last been perfectly well on December 4, when a severe infection of the upper respiratory tract developed with a "high" temperature. He remained in bed for eight days, and on getting up complained of general malaise, which persisted. On December 17, vision began to fail in the nasal field of the right eye, and in five days he was totally blind in this eye. On December 23, he could not see objects clearly in the temporal side of the left eye. In three days vision failed completely. The loss of vision was not associated with headache or dizziness. During the period when vision was diminishing he complained that movements of the eyes from side to side caused pain. When vision was completely lost, pain on movement disappeared.

For two years the patient had worked as a clerk in the post-office. He drew well and had been allowed to paint the signs required. This extra work he usually carried out during the lunch hour, and it had been his custom to eat lunch in the workroom without particular care as to the paint on his hands. This was the only history that he could give of exposure to lead. He was married. His wife was alive and well and had never had a miscarriage. He had two children, aged 3 and 5. Sexual activity had continued as usual up to the time of admission, and from his description libido and potency were normal. His usual weight was 193 pounds (87.5 Kg.), the weight on admission. The past medical history contained nothing of note, and the family history was not relevant.

Examination.—The patient was completely blind. The pupils were round, equal and dilated. They did not react to light. The right optic disk was pale, and the left showed some pallor. The other cranial nerves were normal. The deep reflexes were symmetrical and normally active. Sensory examination gave normal results in all modalities. Muscular strength was good throughout. He cooperated well, and the emotional reactions to his situation were such as might be expected.

The systolic blood pressure was 162; the diastolic, 88. The skeletal system was normal. The gums showed no lead line.

Laboratory examinations showed: The Wassermann reaction of the blood was negative. The red blood cell count was 3,390,000, with 65 per cent hemoglobin

2. Fairhall, L. T.: Lead Studies: VIII. The Microchemical Detection of Lead, J. Biol. Chem. **57**:455, 1923.

(Tallqvist). The white blood cell count was 4,500, with a differential count of 62 per cent neutrophilic leukocytes, 30 per cent small lymphocytes and 8 per cent large lymphocytes. No abnormality was observed in the form or staining of the red blood cells. The urine showed nothing of note.

The Wassermann reaction of the cerebrospinal fluid was negative. The pressure was 120 mm. of water. There were 5 cells per cubic millimeter.

Roentgen examination was made by Dr. Ross Golden; he reported that stereoscopic plates of the skull showed the sella turcica to be markedly enlarged, the floor depressed and the posterior clinoids much thinned. The right anterior clinoid had practically disappeared. The left was eroded. It seemed as though there might be some erosion of the lesser wing of the sphenoid on the right. The sinuses and the rest of the skull were normal. Roentgenograms of the optic canals, taken by Dr. H. H. Goalwin, showed that the left canal was normal, but the lower outer wall of the right canal was eroded. A diagnosis of an expanding lesion in the sella turcica was clear from the roentgenograms.

Treatment and Course.—In spite of the roentgen findings, it was thought that the failure of vision was too rapid to be due to a pituitary tumor. The manner in which the visual loss occurred suggested retrobulbar neuritis of toxic origin. Dr. Ward A. Holden believed that alcohol could be ruled out and suggested, even though complement-fixation tests were negative, that vigorous antisyphilitic treatment be carried out. The patient was given a course of neoarsphenamine and potassium iodide.

On Jan. 2, 1926, the patient began to see flashes of light and to complain again that looking to either side caused pain. On January 10, he felt that he could see light in the left visual field of the right eye. He was able to detect the direction of movements of the hands on January 11, and the right pupil reacted to light, and there was a consensual reaction from left to right. The left pupil did not react to light directly. Questionable perception of light was present in the temporal field of the left eye on January 20. He was discharged from the hospital on January 25 with instructions to continue taking potassium iodide, 15 grains (0.972 Gm.) three times a day, and to report to the outdoor department for further antisyphilitic treatment.

Shortly after discharge from the hospital, it was reported that 1.1 mg. of lead had been found in the feces collected during hospitalization two weeks after potassium iodide had been started.

The patient returned for further study on February 14. Vision in the meantime had improved so that he could recognize persons fairly well, and examination of the visual fields showed large central scotomas in both eyes, with full peripheral fields. Both optic disks showed marked atrophy. These findings convinced Dr. M. J. Schoenberg that the patient's visual difficulty was due to retrobulbar neuritis and not to a tumor. Dr. F. B. Flinn examined the cerebrospinal fluid for lead and with Fairhall's hexanitrite method demonstrated hexanitrite crystals of lead in it. No crystals were found in control tests which Dr. Flinn made simultaneously. It then seemed likely that the blindness was due to lead poisoning. However, no stippled cells were found in the blood, and no lead line was present on the gums.

During this period the patient complained of tingling in the lower extremities. Careful neurologic examination revealed no objective sensory changes, pathologic reflexes or weakness of any muscle groups. Antisyphilitic treatment was stopped. Potassium iodide was continued. He was discharged on February 25, with the diagnosis of pituitary tumor, lead poisoning and retrobulbar neuritis.

Readmission.—On March 2, five days after discharge from the hospital, the patient was readmitted complaining of inability to void, obstipation and great weakness and marked numbness and tingling in the legs. He gave the history that on the afternoon following discharge from the hospital he had taken a long walk, at the end of which he was so tired he was barely able to reach home. The legs tingled and felt very weak. During the next three days the numbness and the tingling and weakness in the legs increased. He began to have difficulty in voiding and finally had to be catheterized. The bowels moved with increasing difficulty.

Neurologic Examination: At the time of readmission all the deep reflexes were present and the same as at the time of discharge five days before. The superficial reflexes, however, were strikingly altered. The cremasteric reflexes were very sluggish, and the lower abdominal reflexes on both sides were absent. The plantar reflexes were of flexion type. There was some hyperesthesia to cotton wool at the lower part of the twelfth thoracic segment; otherwise, sensibility to touch was normal. Temperature sensation was diminished at the level of the eighth thoracic segment. Below this level there was hyperesthesia. Pain was diminished at the junction of the tenth and twelfth thoracic segments, and below this there was marked hyperesthesia. There was no loss of muscular power in the arms. The legs, however, were weak, and the patient was able to stand only with difficulty. After standing, the muscles of the left calf contracted powerfully and remained contracted for almost one minute. He did not complain that this was painful.

The patient was unable to void and had to be catheterized. The temperature, pulse rate and respiration were normal. The white blood cell count was 15,330, with 50 per cent polymorphonuclear leukocytes, 45 per cent lymphocytes, 4 per cent mononuclears and 1 per cent transitional cells.

The spinal fluid pressure was 170 mm. of water. The fluid was perfectly clear; a faint white pellicle formed on standing. There were 7 cells per cubic millimeter, 5 lymphocytes and 2 polymorphonuclear leukocytes. The globulin test was negative. The total proteins were 113 mg. per hundred cubic centimeters. The fluid was again examined for lead by Dr. Flinn, as well as a specimen of urine, and he reported that lead was present in both.

Further Course.—With the development of these new symptoms, vision showed no apparent change. The central scotomas were readily demonstrable, and rough tests showed the visual fields normal in outline.

The symptoms of an ascending myelitis rapidly developed. By the third day after admission, all the deep reflexes were gone in the legs and the legs were completely paralyzed. The cremasteric response was very sluggish. The Holmes flexion flexor reflex was present on both sides, but was more marked on the left.

Tactile sensation was slightly diminished up to the seventh thoracic segment on the left; on the right it was lost up to the tenth thoracic segment and diminished up to the sixth and seventh segments. Pain was markedly diminished on the left up to the junction of the sixth and seventh thoracic segments. On the right side it was lost up to this level. Temperature sensation was completely lost below the tenth thoracic segment, diminished from the tenth to the sixth thoracic segment and normal above the sixth.

It was decided that potassium iodide had discharged stored lead into the circulation more rapidly that it could be excreted. On March 6, the procedures outlined by Aub, Fairhall, Minot and Reznikoff to store lead were begun. The patient was given 15 cc. of a 5 per cent solution of calcium chloride intravenously, as much milk as he could take and calcium lactate by mouth. The rapid progres-

sion of signs stopped. On March 9, though the spinal fluid contained 500 cells, 93 per cent of which were lymphocytes, and the total proteins were 277 mg., Dr. Flinn could no longer find lead hexanitrite crystals in it, and no lead could be demonstrated in the urine. Following the institution of calcium therapy, the level of involvement of the spinal cord moved one segment higher, to include the fifth thoracic segment. From March 13 until death on August 18 from infected bed sores and pyelitis, the patient was given a diet high in calcium. In spite of the

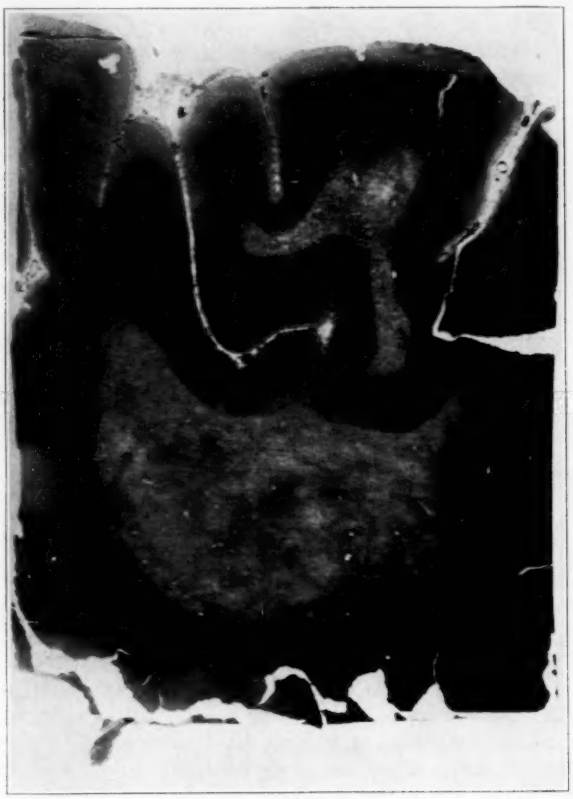

Fig. 1.—Cerebrum. Plaque of glial scarring and loss of myelin. Axis-cylinders were present in the plaque. Fat-laden phagocytes filled the area. Weigert-Pal stain. The lead content of a similar plaque from the cerebrum was 0.817 mg. per hundred grams, wet weight, while the normal-appearing brain showed 0.032 mg. of lead.

infection, no recrudescence of signs took place, in regard either to vision or to myelitis.

Postmortem Examination.—This was performed by Dr. Benjamin Vance of the Medical Examiners Department in New York. He gave us helpful cooperation, and Dr. Charles Norris, Chief Medical Examiner of New York City, gave us permission to report the observations. Dr. Vance's anatomic diagnosis was: myelomacia of the lower part of the spinal cord; neoplasm of the hypophysis;

decubital ulcers; pseudomembranous cystitis; ulcers of the rectum; bronchopneumonia. Chemical examination was made of specimens of bone and liver, and Dr. A. O. Gettler reported that they contained lead.

We were permitted to examine the brain and spinal cord. The specimen was fixed in solution of formaldehyde, U. S. P. (1:10) in a clean glass brain jar. The following points summarize our observations:

The spinal cord was flattened and soft up to the fifth thoracic segment. Above this it was firm. The leptomeninges showed white cartilaginous flakes in the lower thoracic and upper lumbar segments; otherwise, they were not unusual. The pial vessels seemed normal. Ascending degenerations were evident in the ascending pathways above the fifth thoracic segment, and the normal architecture was maintained. At the fifth thoracic segment, where the right posterior horn joined the right anterior horn, there was a small cavity, and the usual markings of the cord were not clear. At all levels below this the normal markings were absent. Small scattered cavities were present, filled with transparent gelatinous material, and myelin was practically absent. Whereas the gray and the white matter were involved above, in the lower lumbar segments the white matter was most altered.

Weigert-Pal stains proved the loss of myelin in the cord. Other stains showed diffuse and widespread evidence of destruction in both the gray and the white matter. The degeneration was not secondary to vascular changes. The only abnormality in the vessels encountered could be explained as a secondary one. Moreover, the microscopic picture did not suggest an infection. Fat-filled phagocytes filled the involved areas. Perivascular collars of round cells were rare. Microscopic examination suggested only a reaction such as occurs with widespread destruction of tissue, much as is seen in traumatic lesions of the spinal cord.

In the cerebral hemispheres (fig. 1) and cerebellum a different picture was present. Here a few focal, sharply circumscribed, firm plaques were present, in which Weigert-Pal stains showed that myelin sheaths were absent. Axis-cylinders could be stained in these. The firmness of the plaque was due to intense glial scarring. Fat-filled phagocytes were still abundant, however. Again nothing was found to suggest that the lesion was of infectious origin.

In the optic nerves and chiasm demyelinized areas were present, also with changes similar to those in the brain.

Dr. Flinn again consented to take charge of the chemical studies of the brain and spinal cord. Areas were taken from normal-appearing brain, brain with plaques, the brain stem, in which no gross abnormality could be identified, and normal-appearing cerebellum and degenerated spinal cord. He also analyzed the tumor, which was a typical chromophobe adenoma of the pituitary body. He found lead in all of the specimens. The results he obtained were as follows:

	Lead in Milligrams per Hundred Grams
Degenerated spinal cord	0.560
Brain with plaque	0.817
Normal-appearing brain	0.032
Normal-appearing cerebellum	0.169
Brain stem	0.134
Tumor	0.962

These estimations were made on wet weights.

Comment.—This case of frank lead poisoning presented the symptoms and pathologic changes of neuromyelitis optica or ophthalmo-

encephalomyelopathy, if Barrera's[3] more recent descriptive term is accepted. The relationship of cases of this type to multiple sclerosis has always been obvious; the etiologic agent has been obscure. This is the first case with which we are familiar in which lead has been proved to be the primary causative factor.

LEAD IN MULTIPLE SCLEROSIS

The study of lead in relationship to multiple sclerosis was begun seriously in November, 1932, when it was discovered that the cerebrospinal fluid of a patient suffering from multiple sclerosis contained lead.

CASE 2.—S. S., a man, aged 30, was seen by one of us in 1923 for Dr. C. F. Martin, and a diagnosis of probable multiple sclerosis was then made. At the age of 8, following diphtheria, he had suffered from weakness of the legs for six months, but recovered. At the age of 15, while doing heavy manual work on a farm, weakness of the legs again developed for a period, and again he recovered; he lost 25 pounds (11.3 Kg.) at that time.

Three months before admission in 1923, while employed in clerical work, he was chronically constipated, with periods of diarrhea and an occasional tendency to retention of urine. He also had paresthesias and relative anesthesia in the was correct. When the patient recovered from the operation, examination of the cerebrospinal fluid showed the presence of lead, and lead was found in the urine.

With the finding of lead in the fluid it was obviously important to make chemical studies on the available autopsy material of proved cases of multiple sclerosis. In only 1 case had precautions been taken to prevent possible contamination of the specimen by lead. In this case we had not been alert to the possibility of lead being present during life, and chemical tests for it had not been carried out. Nevertheless,

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3. Barrera, S. E.: Ophthalmo-Encephalo-Myelopathy: Clinico-Pathological Study of a Case, Psychiatric Quart. **6**:421, (July) 1932.

trunk and limbs and involuntary jerkings of the legs, especially when falling asleep.

The fundi were normal. The tendon jerks were active. There were bilateral plantar extensor reflexes. The abdominal reflexes were absent. The gait was spastic. The Wassermann test with the blood and cerebrospinal fluid was negative.

In 1927, on account of the relative anesthesia in the trunk, with a possible upper level, a laminectomy was performed in another city but no block was found. The patient, however, improved greatly some months after this operation. In the autumn of 1932, the legs again became spastic, especially the left. The patient showed nystagmus and slight intention tremor, and was somewhat overlabile emotionally. Wassermann tests with the blood and cerebrospinal fluid were negative. There were no cells in the spinal fluid; the total proteins were 65.7 mg. per hundred cubic centimeters; the colloidal gold curve was 1211120000. Again a laminectomy was performed in the thoracic region. The size of the cord was noted as small, and slight meningeal adhesions were found. Later there developed a transient weakness of the right hand.

It was obvious that the initial diagnosis of multiple sclerosis, made in 1923,

at autopsy, a portion of the cord had been placed in chemically clean glass bottles, fixed in formaldehyde that was proved to be free from lead, and sealed with paraffin-coated corks. When the opportunity for critical chemical analysis presented itself in November, 1932, the specimen was found to contain 0.13 mg. of lead per hundred grams, wet weight, or 0.55 mg. of lead per hundred grams, dry weight.

CASE 3.—*History.*—A. R., a woman, aged 30, who was admitted to the neurosurgical service of Dr. W. Penfield on March 2, 1931, stated that five years before, about nine months after the birth of her first child, she had what she described as an ache in the right leg, which lasted for one day. She had no further

Fig. 2 (case 2).—Cerebral cortex. Patches of demyelinization, while more frequent in the white matter, were also present in the gray matter of the brain, and it is interesting that the nerve cells were preserved in large part in the areas showing loss of myelin. Weigert-Pal stain.

unusual symptoms until four months after the birth of the second child, two years before examination, when numbness of the same leg developed. One year later, during the third pregnancy, weakness of the leg came on, and the numbness spread to involve the whole leg. Control of the bladder and sphincteric control became imperfect, and there was marked urgency. In November, 1930, urgency and frequency became more troublesome. She had been unable to check the flow of urine since that time. She had realized when the bowels were ready to move, but had no power to stop or to start them.

Examination.—The cranial nerves were normal. There was a definite spastic paresis of both legs, with bilateral plantar extension and absence of the abdominal reflexes. Sensation in all forms was impaired over the lower extremities and

trunk up to the fifth thoracic segment; also over the right eighth cervical dermatome; all forms of sensation were diminished. In the lower extremities tactile sensation was less affected than pain and heat and cold sensibility. Vibratory sense was absent in the toes, and was recognized faintly over the legs, but was not normally appreciated until the first thoracic vertebral spine was reached.

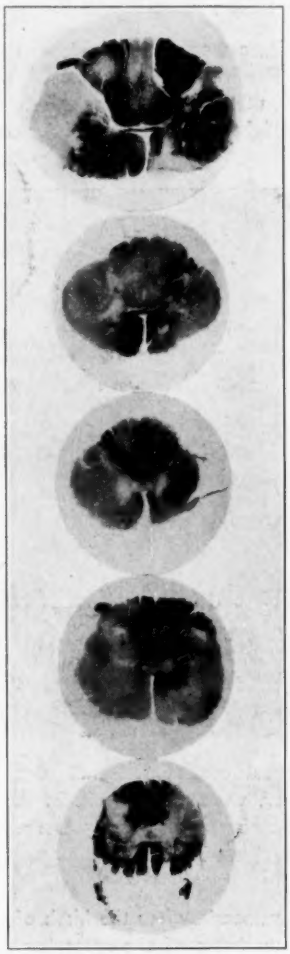

Fig. 3 (case 2).—Spinal cord. Multiple disseminated patches of demyelinization are present. Some tracts show secondary degeneration; others do not. The cord contained 0.13 mg. of lead per hundred grams by wet weight and 0.55 mg. by dry weight. Weigert-Pal stain.

The red blood cell count was 4,380,000; the hemoglobin, 85 per cent (Sahli); and the white cell count, 5,000. Free hydrochloric acid was present in the stomach. The Wassermann test was negative with the blood and cerebrospinal fluid. The total proteins in the cerebrospinal fluid were 66.9 mg. per hundred cubic centimeters; 10 lymphocytes per cubic millimeter were present.

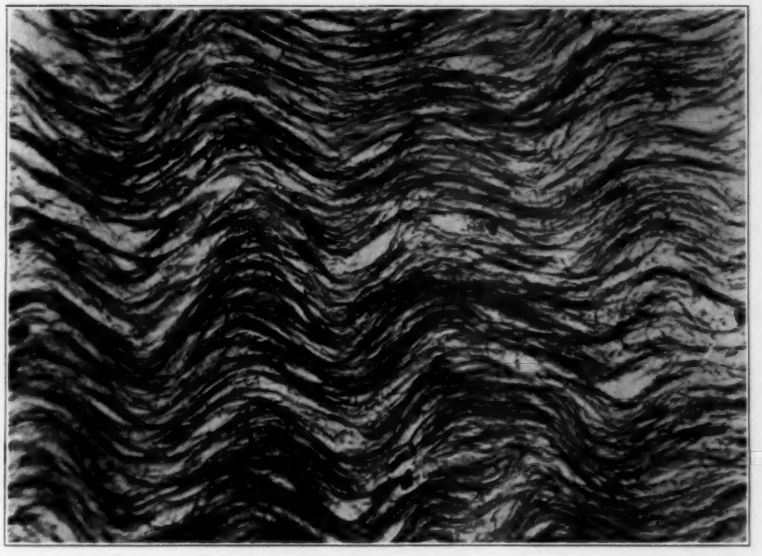

Fig. 4 (case 2).—Longitudinal section of spinal cord. In old plaques in the spinal cord, the gliosis was marked, and glia fibers arranged themselves in wavy parallel lines. Phosphotungstic acid-hematoxylin stain.

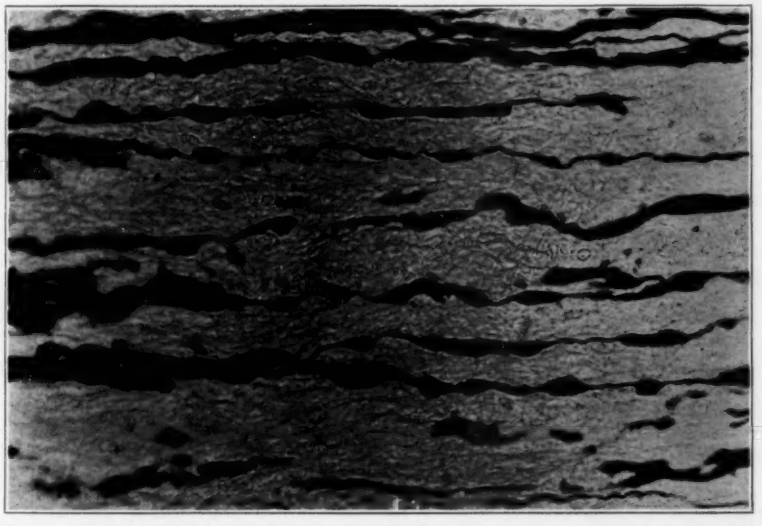

Fig. 5 (case 2).—Spinal cord. Longitudinal section, taken from the same plaque as shown in figure 4. The axis-cylinders are numerous. They show irregular beading and frequent large varicosities. Gros-Bielschowsky stain.

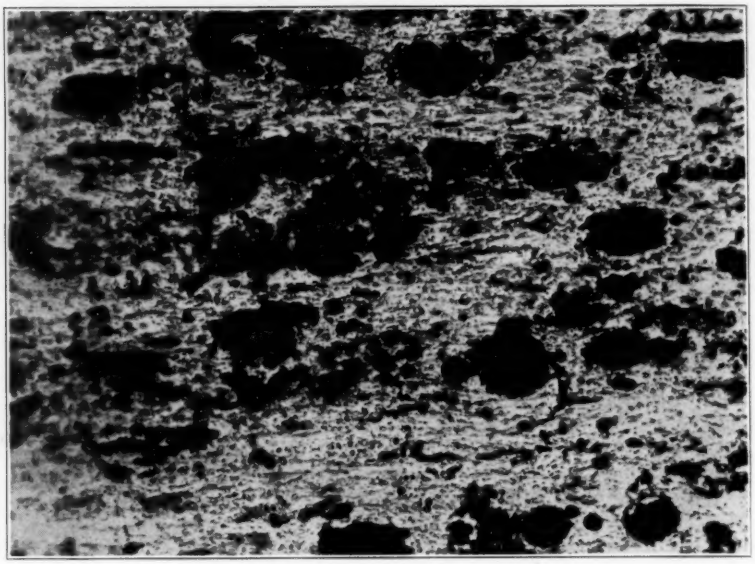

Fig. 6 (case 2).—Spinal cord, longitudinal section. The earliest stage of the breaking up of myelin into neutral fat is seen. Small granules of fat are present in the medullary tubes. Some large phagocytes laden with fat are present. Scarlet red stain.

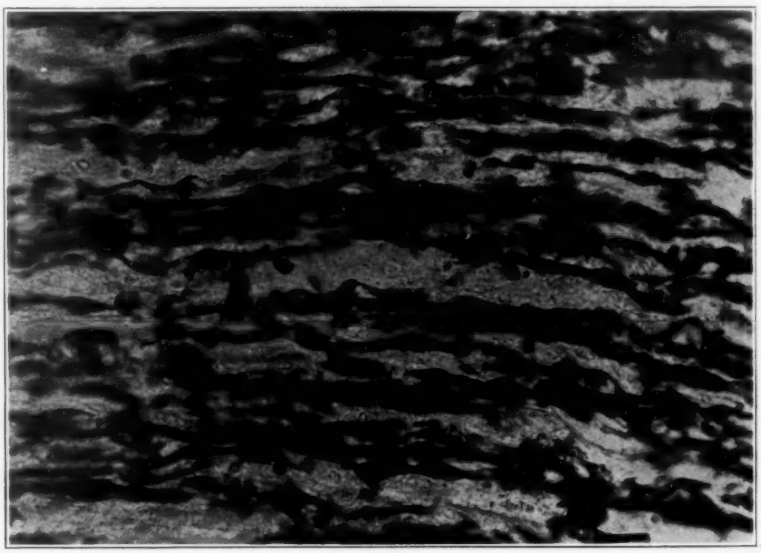

Fig. 7 (case 2).—Spinal cord, longitudinal section, from the same area as figure 6. The medullary sheaths show great irregularities. Weigert-Pal stain.

Course.—During the period of hospitalization the disability progressed. On one occasion the patient suddenly became blind. She then slept for six hours and on awakening could see again. She died on Oct. 4, 1931, in a home for incurables.

Necropsy.—The postmortem examination was made by Dr. William Chase of the pathologic department. The chief anatomic diagnosis was: pyonephrosis, bilateral with calculi; exudative purulent cystitis; productive pleurisy; passive hyperemia of the liver.

The brain and spinal cord were studied in the neuropathologic department. On gross examination of the cord the diagnosis of multiple sclerosis could be made. Irregular areas of atrophy, which varied in consistency from firm to moderately soft plaques, were present in the spinal cord. In the white matter of the cerebellum and in the white matter adjacent to the ventricular walls a few small grayish plaques could be identified.

From the microscopic standpoint, the lesions were typical of multiple sclerosis. Recent and old areas of demyelinization were encountered throughout the cerebral hemispheres, the cerebellum, the optic nerves and chiasm and the spinal cord (figs. 2 and 3). In the spinal cord, the older plaques were made up of dense glial scars, with glia fibers arranged in parallel lines (fig. 4). In such areas Weigert-Pal stains showed that myelin was gone, but Gros-Bielschowsky stains showed nerve fibers with many varicosities still present in the scar (fig. 5). In more recent areas of loss of myelin, the neuroglial reaction was much less marked, and fat-filled phagocytes packed these areas.

The earliest changes which could be made out in myelin were the collection of fine fat granules in the myelin sheaths (fig. 6). Weigert-Pal stains in such areas (fig. 7) revealed unusual varicosities in the myelin tubes, the significance of which would not have been apparent if fat stains had not shown the change and indicated that further studies should be carried out.

Comment.—The patient gave no history of lead poisoning, and later inquiry from the patient's family disclosed no obvious exposure to lead. We therefore can point out only that the amount of lead found in the spinal cord is almost as great as that recorded in the literature in patients with typical lead encephalopathy and call attention to the fact that pregnancy and lactation are important factors in mobilizing calcium. Since stored lead behaves as calcium does, lead would be discharged into the blood stream in a soluble form and this might well be responsible for the exacerbations so commonly observed in multiple sclerosis. Gowers,[4] for instance, recorded a case which began during pregnancy, remained stationary until the next pregnancy and then became progressive.

In view of these findings and considerations it appeared that lead might well be a cause of multiple sclerosis. The challenge was obvious, and our line of attack was as follows, although the exigencies of the patient's circumstances and the conditions of the service have sometimes interfered with the plan in some of its details:

4. Gowers, William: A Manual of Diseases of the Nervous System, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1903, vol. 2, p. 544.

CLINICAL PROCEDURE

In taking the history special attention was given to any account of putting toys in the mouth in infancy and eating the paint off the cot in childhood, chewing pencils and crayons during school life, and later any possible exposure in an occupational way.

In the examination the lead line on the gums was looked for, and the blood was examined for stippled cells.

On admission the patient received a purge, and the urine and stool for three days were collected in specially cleaned and prepared receptacles and sent directly to the laboratory.

The cerebrospinal fluid was tested for lead. On admission it was collected in pyrex test tubes especially cleaned in the laboratory. The pressure of the cerebrospinal fluid was noted, and evidence of spinal block was excluded; the number of cells per cubic millimeter, the presence of globulin and the total protein content were estimated in the usual way, and the Wassermann reaction with blood and spinal fluid was tested.

Following this, except in the presence of contraindications, the patient was put into a state of acidosis by the administration of ammonium chloride up to 2 Gm. in water, twelve times a day. At the same time he was given a diet low in calcium by excluding milk, cheese, vegetables, fruit and eggs, and the bowels were kept active.

The carbon dioxide-combining power of the blood was taken frequently, often two or three times a day when we feared an exacerbation of symptoms. The appearance of headache, generalized pains, general malaise and sometimes vomiting were, as a rule, warnings to lighten the medication. It was our wish to keep the patient in a state of acidosis over a more or less prolonged period, but this was not always practicable and we had to be content with what was possible.

During the state of acidosis, the excreta were again collected with the same precautions, and the cerebrospinal fluid was again taken. If lead was present in the tissues it should be much increased in the excreta and the spinal fluid during this period, and our results have not disappointed us in this respect.

In the third period, the ammonium chloride was stopped, and the patient was given a diet high in calcium and calcium was administered. We tried various methods, both intravenously and by mouth; at the same time food rich in vitamins was given, and when the alkaline reserve was restored the excreta and spinal fluid were again collected for examination.

CHEMICAL METHODS

Urine and Stools.—The analytic methods used in these studies have been those developed by Aub, Fairhall, Minot and Reznikoff,[1] with minor modifications.

Both urine and stools were analyzed, so far as possible, in three day periods, and the results obtained have been calculated on this basis. The excreta were collected in glass containers previously cleaned with dilute nitric acid and distilled water.

The lead in the urine was precipitated by entrainment with the phosphates, by the addition of an excess of ammonia to the fresh urine. Specimens of stools were dried on the steam bath, and then weighed and analyzed as follows:

The precipitated phosphates, with any entrained lead, or the dried stool was ashed in silica dishes in an electric muffle furnace at a temperature not exceeding 450 C. The ash was dissolved in dilute hydrochloric acid and carefully neu-

tralized with sodium hydroxide to a slightly acid reaction. Hydrogen sulphide was passed into the solution in a 50 cc. centrifuge tube, at room temperature, to precipitate the lead as the sulphide. The precipitated sulphides were carefully washed with 0.1 per cent hydrochloric acid saturated with hydrogen sulphide.

After washing, the lead sulphide was dissolved in nitric acid and, after removal of any hydrogen sulphide by boiling, was carefully neutralized with sodium hydroxide and acetic acid to a slightly acid reaction. The lead was then precipitated as the chromate. The lead chromate was filtered off and washed free from soluble chromates. The precipitate was dissolved in dilute hydrochloric acid in a large test tube. Potassium iodide solution and starch were then added, and the free iodine was titrated against thousandth-normal sodium thiosulphate (1 cc. of thousandth-normal sodium thiosulphate equals 0.069 mg. of lead).

The results so obtained have been calculated on the basis of three day periods and have been expressed as milligrams of lead per liter of urine, or per hundred grams, dry weight, of stool.

Precautions: Since the quantities of lead which have been determined are so small, strict precautions in all the analytic work have been observed. Among these, the following are the most important: (1) reagents which were not found to be free from lead have been purified; (2) all silica dishes and all glassware, including the containers for the excreta, were carefully cleaned with nitric acid and distilled water; (3) precautions were taken throughout to prevent contamination from dust and other possible sources.

Cerebrospinal Fluid.—For the microchemical detection of lead in the cerebrospinal fluid, the original method of Fairhall [2] has been used, with minor modifications.

At least 5 cc. of the fluid in a silica crucible was evaporated to dryness on the steam bath, with the addition of a few drops of redistilled nitric acid to facilitate destruction of the organic matter. The residue was ashed completely in a muffle furnace at a temperature of not over 450 C. The ash was dissolved in dilute hydrochloric acid and transferred to a 15 cc. centrifuge tube. The lead was precipitated as the sulphide, as for urine and stool. Inorganic salts were removed by several washings with 0.1 per cent hydrochloric acid saturated with hydrogen sulphide. The lead sulphide was then dissolved in 2 drops of concentrated nitric acid.

For preparation of a slide, about one fourth of a drop was carefully evaporated to dryness on a microscope slide. Minute amounts of sodium acetate and copper acetate solutions were then added from micropipets and evaporated to dryness, resulting in a ring of salts about 2 or 3 mm. in diameter. The slide was then chilled, and a very minute amount of dilute acetic acid and a tiny crystal of potassium nitrite were then added.

When such a slide is examined microscopically, crystals of lead hexanitrite ($K_2Cu\ Pb\ [NO_2]_6$), if present, appear as brown or black squares or cubes readily distinguishable from the blue crystals of the copper salts or the colorless ones of the sodium or potassium salts. The sensitivity of the test may be gathered from the fact that three definitely positive slides, each containing from 20 to 30 tiny hexanitrite crystals, may be prepared from 5 cc. of a synthetic spinal fluid containing 0.001 mg. of lead.

Since the test is so sensitive, the following special precautions have been observed in addifion to the general ones already mentioned: (1) the nitric and hydrochloric acid, as well as the distilled water, have been redistilled from an all glass pyrex still; (2) all reagents have been carefully tested for lead; in addition, uniformly negative slides have been prepared, at frequent intervals, the

reagents alone being used; (3) potassium nitrite has been described by Weller and Christensen [5] and others as containing small amounts of lead. The chemically pure (analyzed) crystals of potassium nitrite we were using gave negative reactions for lead on all occasions. Nevertheless, to make doubly sure, these crystals were recrystallized following Fairhall's technic.

Case 4.—A. S., a man, aged 31, was admitted to the hospital in February, 1933. A diagnosis of multiple sclerosis had been made by Dr. A. H. Gordon, of Montreal, in 1925, and confirmed in many clinics since.

The illness began in about 1918, at the age of 16, with numbness in the right hand. This condition was diagnosed as neuritis and disappeared in two or three months, to recur again in the left foot and up to the knee; after some time the numbness disappeared. It came and went. Then a tight feeling about the chest developed, and also a spasticity of the legs. For the past three years the patient

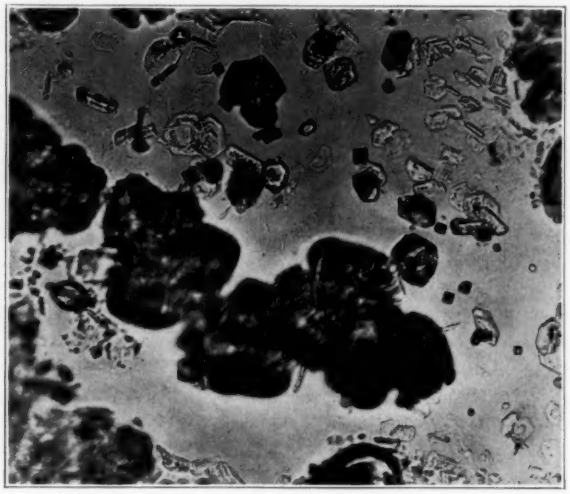

Fig. 8 (case 4).—Hexanitrite crystals of lead from the spinal fluid.

had hardly been able to walk. During December, 1930, the face was pulled to the right for three weeks; then it recovered completely. For four months (1931) the patient could not see with the right eye, and found it difficult to lift the right foot from the ground. This improved, and the left foot then became involved. For three months there were dizziness and slight headache, some vomiting and considerable constipation, with a tendency to precipitancy of micturition.

On examination there were a slight pallor of the temporal halves of the optic disks; some lateral nystagmus; marked intention tremor of both hands; marked spasticity of the legs, with increased tendon jerks and ankle and patellar clonus;

5. Weller, C. V., and Christensen, A. D.: The Cerebrospinal Fluid in Lead Poisoning, in The Human Cerebro-Spinal Fluid, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1926, vol. 4, chap. 29, p. 464.

absence of the abdominal reflexes, and bilateral plantar extension. There were also definite loss of sense of position and loss of vibration sense in the legs.

Examination for Lead.—In this case it was possible to follow the outlined clinical procedure fairly completely. Hexanitrite crystals of lead were demonstrated in the cerebrospinal fluid before the patient was put in a state of acidosis (fig. 8). During acidosis, 100 cc. of spinal fluid was withdrawn, the technic followed in encephalography being used. Hexanitrite crystals of lead were readily demonstrated, but the amount of lead was too small to estimate quantitatively, since the lower practical limit of the chromate method of the Harvard workers[1] is about 0.04 mg. of lead; the quantity present in the 100 cc. of spinal fluid was, therefore, less than this amount. The spinal fluid was examined for lead seven different times and was found positive on every occasion. The spinal fluid also showed from 135 to 75 mg. per hundred cubic centimeters of total protein. Pandy's test was negative, and there were from 30 to 10 lymphocytes per

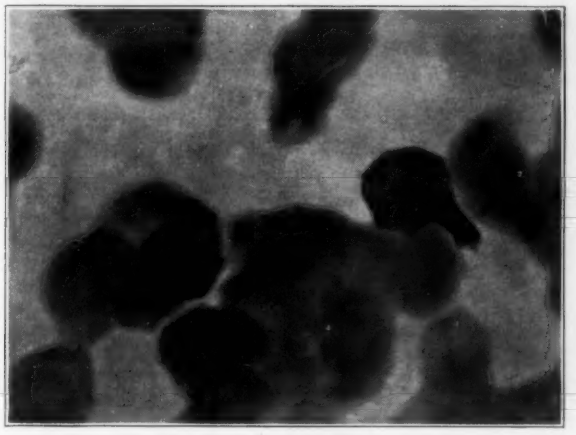

Fig. 9 (case 4).—Basophilic granules in a red blood cell.

cubic millimeter. This fall in total proteins and in the number of lymphocytes took place under administration of calcium.

The Wassermann test was negative with the blood and the cerebrospinal fluid.

The blood on several occasions showed stippling of the red cells (fig. 9), and during acidosis there were periods when these cells were more easily found.

The large amount of data obtained on the excreta is best summarized in table 1. The excretion of lead is here reported for sixteen three day periods. The prompt increase in elimination in both urine and stool under acidosis is apparent. Although during the period of acidosis the output per liter in the urine dropped to 0.01 mg., there was an increase in total excretion, as the urinary output for this period was 7,500 cc. Under administration of calcium, excretion gradually decreased, though irregularly; for successive periods there was no urinary output of lead. The graph of the excretion of lead (fig. 10) visualizes the results.

We hoped that with the administration of calcium lead would disappear from the spinal fluid as it did in case 1. To date this has not happened. It is true that the number of crystals that can be demonstrated now are much fewer, but it is obvious that it is unsafe to use this delicate qualitative method in a quantitative way.

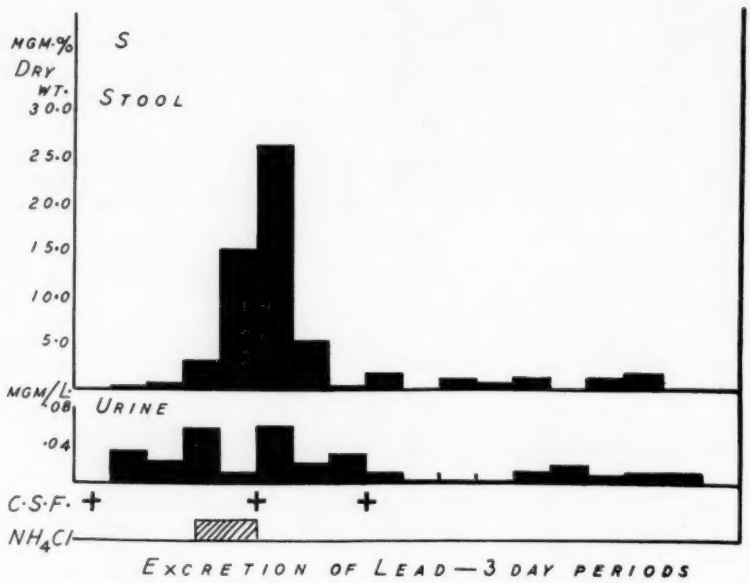

Fig. 10.—Graph of the excretion of lead plotted from the data in table 1. The excretion of lead rose to 26.1 mg. in the stools. The cerebrospinal fluid was positive for lead before, during and immediately after acidosis.

TABLE 1.—*Excretion of Lead in Case 4 (Calculated on the Basis of Three Day Periods)* *

Period	Urine, Mg. per Liter	Stool, Mg. per Cent (Dry)	Urine Total, Mg.	Stool Total, Mg.	Approximate Total Output
1	0.034	0.08	0.10	0.20	0.30
2	0.023	0.62	0.10	0.60†	0.70†
3‡	0.058	3.02	0.32	1.48	1.80
4‡	0.010	15.20	0.05	3.00†	3.05†
5	0.060	26.10	0.12	12.42†	12.54†
6	0.020	5.11	0.03†	3.06	3.09
7	0.030	0.26	0.06	0.12	0.18
8	0.010	1.62	0.02	0.30	0.32
9	.....	None	....	None	
10	.....	1.20	0.01	0.76	0.77
11	0.003	0.60	0.01	0.47	0.48
12	0.012	1.22	0.02	0.96	0.98
13	0.018	None	0.07	None	
14	0.007	1.20	0.02	0.18†	0.20
15	0.010	1.60	0.03	0.30	0.33
16	0.010	None	0.01	None	

* Note the marked increase in the excretion of lead in the stools during acidosis and the period immediately following it.

† Approximate value only.

‡ Period of acidosis (ammonium chloride).

During acidosis the patient complained of headache and pains all over, and he vomited. When the carbon dioxide-combining power reached 41.5 per cent, the acidosis was stopped and calcium administered. The intention tremor in the hands was increased while he was in a state of acidosis. After he had been on calcium therapy for some time he could sit up in bed much more easily and touch his knee with the heel, which he had not been able to do for some time.

At the age of 11 the patient began to work in a dry-goods shop. He learned there to test the fastness of colors in silks by moistening them with his tongue. He had continued this practice ever since, although he had realized that the silks were leaded. Samples of the silks from his stock cast a shadow under the fluoroscope. Fairhall and Heim [6] have demonstrated that these leaded silks are not a hazard to the wearer, but one can imagine that they would become a source of poisoning if licked frequently.

CASE 5.—Mrs. C., aged 33, referred by Dr. A. A. MacKay of Montreal, who was admitted to the hospital on Feb. 17, 1933, showed an almost complete absence of free hydrochloric acid in the gastric secretion and marked anemia.

On February 25, examination of the blood by the hematologic department showed 3,100,000 red cells, 8,000 white cells, 79 per cent hemoglobin (11.1 Gm. per hundred cubic centimeters), a color index of 1.27, and 4 per cent reticulocytes. The question of pernicious anemia in a moderate hematologic remission was considered, and the patient was given intravenous liver therapy. The blood when examined again on March 10 showed 4,340,000 red cells 6,100 white cells, 80 per cent hemoglobin (11.20 Gm. per hundred cubic centimeters), a color index of 0.9 and 2 per cent reticulocytes. As there was no increase in the reticulocytes after liver therapy, it was decided that the condition was probably not pernicious anemia and might be anemia secondary to lead. Dr. Joseph Kaufmann reported a few cells showing doubtful stippling. The clinical history was characteristic of multiple sclerosis, and it was worth considering whether or not the blood picture might not be the result of lead poisoning.

Two years ago, after an operation for ovarian cyst, and six weeks after return home, the patient lost the use of the hands for several months. She was well until six months ago, when extreme weakness developed in the right leg, followed by more or less sudden weakness in the left leg; later still there were sudden weakness and spasticity from the waist down.

Clinically, there was some pallor of the temporal sides of the optic disks. There were also nystagmus on lateral movement of the eyes, impaired vibration sense and loss of sense of position in the lower extremities, with marked spasticity. The tendon jerks were exaggerated, and the plantars showed a bilateral Babinski phenomenon. The abdominal reflexes were absent, and there was precipitancy of micturition.

Examination for Lead.—Lead was found in the spinal fluid. The total proteins were 48 mg. per hundred cubic centimeters, and there were 2 lymphocytes.

Over the first three day period, the urine showed 0.028 mg. per liter. On March 13, ammonium chloride was begun and was continued until March 22, when the carbon dioxide-combining power was 30 per cent by volume. There was a prompt increase in the output of lead, especially in the stools, although much less marked than in case 4. During the first period of acidosis, 3.2 mg. was excreted

6. Fairhall, L. T., and Heim, J. W.: Problem of Possible Health Hazard of Lead-Weighted Silk Fabric, J. Indust. Hyg. **14**:317 (Nov.) 1932.

with little change in the amount in the urine, although there was a drop in the amount per liter as the volume was doubled (fig. 11 and table 2). On March 22, the spinal fluid was again found positive for lead.

On March 23, the patient was given a diet high in calcium, but her circumstances made it necessary for her to leave the hospital, and it was impossible to test the excretion further. Ten days later the cerebronspinal fluid still showed some lead.

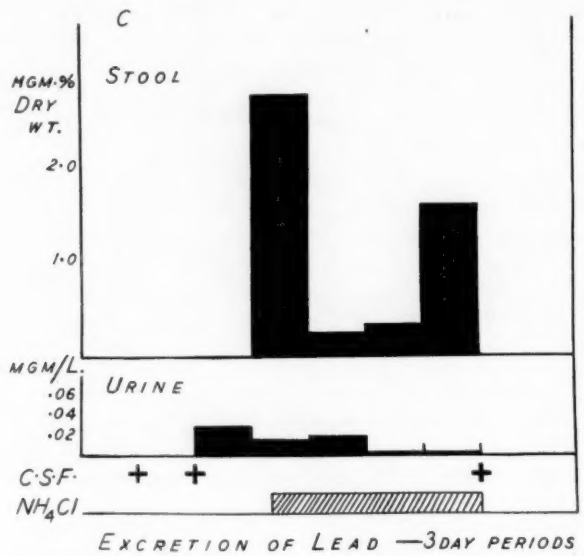

Fig. 11.—Graph of the excretion of lead plotted from the data in table 2. The excretion of lead in the stools during acidosis rose to 2.7 mg. The cerebrospinal fluid was positive for lead before and during acidosis.

TABLE 2.—*Excretion of Lead in Case 5 (Calculated on the Basis of Three Day Periods)* *

Period	Urine, Mg. per Liter	Stool, Mg. per Cent Dry Weight	Urine Total, Mg. Pb	Stool Total, Mg. Pb	Approximate Total Output
1.....	0.028	None	0.14	None	
2‡.....	0.014	2.7	0.09	3.10†	3.2†
3‡.....	0.018	0.25	0.08	0.35†	0.4†
4‡.....	Negative	0.33	Negative	0.38	0.4
5‡.....	Negative	1.58	Negative	1.20	1.2

* The increase in the excretion of lead during acidosis was much less than in case 4.
† Approximate value.
‡ Administration of ammonium chloride.

In this patient the spinal fluid has been examined on four separate occasions, and lead has been demonstrated every time. We think that it was present in smaller quantities at the last examination.

CASE 6.—Miss G. S., aged 24, who was admitted to the hospital on March 21, 1933, had had the symptoms and signs of multiple sclerosis for four years. She complained of inability to walk without help, and a heavy feeling in the legs from

the hips down. She had been employed as a stenographer and in clerical work since the age of 18.

The present illness began in 1927, at the age of 18. While in bed, under treatment for a toxic goiter, she complained of paresthesias and pain in both legs, so that she could not tolerate the weight of the blankets. Both legs were involved from the knees down. This lasted about two weeks and disappeared. In May, 1929, sight in the right eye became suddenly impaired, but the condition cleared up again in about two months and then recurred a year later. In July, 1931, while picking berries, she suddenly complained of heaviness of the feet and legs. There was no pain or numbness, and the heavy feeling passed off in three or four hours. In September, 1931, paresis of the muscles of the right ankle developed, so that she could flex it only with the greatest difficulty. There was no pain, and the weakness passed off in a few hours. From this time on, weakness kept recurring from time to time, the left ankle becoming similarly affected though not to the same extent, and she began to have a heavy feeling in the back. The patient found that she was apt to stumble and fall, and walking had been getting more and more difficult. Since July, 1932, she had had a coarse tremor in the left hand when she tried to use it, and some paresthesia in the right hand. Constipation had been marked for the past year or so, and there had been some difficulty in micturition, with a tendency to retention.

She was an only child. She had measles and chickenpox in childhood; tonsillectomy was performed when she was 10 years old, appendectomy at 17 and thyroidectomy at 18 or 19. Menstruation stopped in March, 1931, with complete amenorrhea for ten months. Since then the periods recurred only every three or four months. There was nothing important in the family history.

Examination.—The positive findings were: marked pallor of both optic disks; slight lateral nystagmus; intention tremor in both hands; marked spastic paresis of both legs; loss of vibration sense and impaired sense of position in both lower extremities; exaggeration of all tendon jerks, with a loss of superficial reflexes, and the presence of a bilateral plantar extensor response.

The Wassermann tests with the blood and cerebrospinal fluid were negative.

The spinal fluid was clear, under slightly increased pressure, and contained 4 cells per cubic millimeter. Pandy's test was negative, but the total proteins were 58.4 mg. per hundred cubic centimeters. The colloidal gold test was negative. The lead hexanitrite test on the spinal fluid was strongly positive. Examination of the blood showed no stippling of the red cells.

Examinations for Lead.—During the first two periods after admission the urine showed an average of 0.01 mg. of lead per liter, and the stools, 0.6 mg. per hundred grams, dry weight. Acidosis was produced very rapidly by the administration of ammonium chloride, bringing the carbon dioxide-combining power down to 34.8 per cent by volume. Unfortunately, there was a tendency to an exacerbation of the symptoms, with failing vision and increased paresthesia of the right hand and more difficulty in moving the legs. It was therefore considered advisable to give a diet high in calcium immediately and to administer calcium by mouth. The amount of lead in the excreta remained practically constant during this short period of acidosis. The cerebrospinal fluid showed a total protein of 60 mg. and was again positive for lead.

CASE 7.—M. G., a man, aged 21, whose condition had been diagnosed as multiple sclerosis in 1929, complained then of paresthesias in the legs, sometimes in the shoulders, and increasing stiffness of the legs. When he attempted to run he would stagger and fall. There was some tremor of the hands. For two years

the condition periodically progressed. In February, 1931, he was in the hospital with an exacerbation of all previous symptoms, and at this time was having occasional periods when vision was blurred. In December, 1932, he was readmitted after an interval during which there had been improvement. The right arm and leg were more stiff, though the left leg was somewhat stronger than it had been. He complained of dizzy spells.

The gait was spastic. The tendon jerks were increased, and there was bilateral ankle clonus. The abdominal reflexes were absent. Both plantar reflexes were of the extensor type. There was some loss of vibratory sense in the lower extremities. The Wassermann reaction was negative in the blood and spinal fluid.

Examination for Lead.—During the first period of observation, while the patient was on a standard hospital diet, the urine showed 0.01 mg. of lead per liter. Unfortunately, the test tube of cerebrospinal fluid collected for the hexanitrite test was lost. The total proteins were 135 mg. per hundred cubic centimeters. The colloidal gold curve was 1212112000.

The patient would not cooperate satisfactorily, and real acidosis was not produced, but the urine showed 0.041 mg. of lead per liter, and the stools, 2.7 mg. per hundred grams. The cerebrospinal fluid was positive for lead. During this partial acidosis the stiffness of the legs was perceptibly increased.

The behavior of the patient was rather difficult while he was in the ward, and he was sent out on a diet high in calcium. He gained 28 pounds (12.7 Kg.) in the first six weeks and improved definitely as far as walking was concerned. The cerebrospinal fluid was collected in the outdoor department. Two different specimens showed lead. Even after three months of a diet high in calcium the hexanitrite test was still positive.

CASE 8.—Mrs. F., aged 39, had been seen by us on various occasions in past years, and the diagnosis of multiple sclerosis was made eight years ago. This had been confirmed many times. She was at her home under the care of Dr. A. W. Young, who had the material collected with the necessary precautions and brought to us for examination.

In 1923, there developed a severe streptococcic infection in the right ankle joint, which had to be incised. During or closely associated with this illness, diplopia developed, which lasted for some weeks. Since that time the illness had run an intermittently progressive course, with repeated ocular paralysis, lasting perhaps for a month or two, and an increasing spasticity of the legs.

Dr. Young reported that the patient showed a coarse nystagmus, speech was distinctly scanning, and she had a marked intention tremor. The legs were very spastic, with increased tendon jerks, patellar and ankle clonus and a bilateral extensor plantar response. The abdominal and epigastric reflexes were absent. There was some involvement of the organic reflexes, which was manifested by precipitancy of micturition and occasional incontinence of feces. There was some loss of sense of position and vibration sense in the lower extremities. The Wassermann reaction with the blood and spinal fluid was negative.

Special Examinations.—Three day specimens of the excreta were obtained in specially cleaned receptacles; the urine showed 0.09 mg. of lead per liter, and the stools, 1.08 mg. per hundred grams, dry weight. The hexanitrite test for lead in the spinal fluid was positive. The examination for total protein was not carried out.

CASES OTHER THAN MULTIPLE SCLEROSIS IN WHICH LEAD WAS FOUND IN THE SPINAL FLUID

Besides the cases of multiple sclerosis, we have had under observation other cases of involvement of the nervous system with the presence of lead in the spinal fluid and in the excreta: 4 cases with symptoms closely simulating cerebral tumor; 4 cases with a localized lesion in the brain stem or cord; 1 case of epilepsy; 1 case of acute polyneuritis following an acute infection of the throat; 1 case of intracerebral hemorrhage in which, post mortem, lead was shown to be present in the bones, liver and central nervous system and 1 case of chronic myositis.

These 12 cases illustrate types of lead poisoning which have recently been described in children [7] and will form the subject of a future report.

The clinical improvement under calcium therapy in 10 of these cases has been gratifying. Lead, however, has not disappeared from the cerebrospinal fluid in the patients when later lumbar puncture has been done.

There are very few instances in the literature in which lead has been demonstrated in the spinal fluid. Since we have found it in 6 cases of multiple sclerosis and in 12 other cases of abnormality of the central nervous system, it is important for us to outline some of the precautions taken in the test and to cite in some detail the cases in which the cerebrospinal fluid has been examined with negative results. Positive slides from synthetic spinal fluid containing known amounts of lead have been prepared to show that lead can be demonstrated when it is present. Control slides have been prepared at frequent intervals, using the reagents alone, and these have been uniformly negative. These points, too, can be mentioned regarding the test. We have found the cerebrospinal fluid positive several times in different specimens from patients who have shown lead. No hexanitrite crystals of lead have been obtained in the cerebrospinal fluid without lead also in the excreta. On the other hand, lead has been frequently found in the excreta of patients in whom the cerebrospinal fluid has shown no lead.

CONTROL CASES

As control cases in which no lead has been found in the cerebrospinal fluid, we have 2 cases diagnosed as multiple sclerosis, both in young adults, with a history of a steadily progressive difficulty in walking, without any sudden onset or exacerbation and no periods of remission. On examination they showed some nystagmus on lateral movement of

7. Children's Memorial Hospital, Montreal, Canada, Symposium on Lead Poisoning in Children, Montreal Medical Chirurgical Society, Canad. M. A. J. **28:** 207 (Feb.) 1933.

the eyes, a slight intention tremor of the hands and a spastic paresis of the legs. The tendon jerks were increased, with ankle clonus, and the plantar reflexes showed bilateral extension. There were also loss of vibration sense in the lower extremities and some impairment of the sense of position. There was no evidence of spinal block. The blood picture was normal, and the gastric secretions showed no abnormality.

Marie [8] described four types of multiple sclerosis on the basis of their mode of progression. These 2 cases belong to his first type, which he described as progressing steadily without exacerbations and without remissions. It will be observed that the cases we have reported with lead in the spinal fluid belong to Marie's second or third types of progression. Though the course has been chronic, they have progressed with exacerbations and have shown remissions.

Besides these, the cerebrospinal fluid has been examined for lead and found negative in 1 case of neuromyelitis optica and 1 case of retrobulbar neuritis; in 3 cases of cerebral thrombosis; in 3 cases of lesions of the pyramidal tract with osteo-arthritic changes; in 5 cases of epilepsy; in 1 case of hysteria; in 1 case of psychoneurosis; in 1 case of essential hypertension; in 1 case of trichiniasis, and in 1 of posttraumatic headache, 20 cases in all.

COMMENT

Metallic intoxication has been suspected as a possible cause of multiple sclerosis by various writers in past years, but the methods of proof have been inadequate and unsatisfactory. As far back as 1883, J. J. Putnam [9] published cases of diffuse lesions of the spinal cord and brain with spasticity of the legs in which he found lead in the urine. He suggested that lead was the etiologic agent. A. Berger,[10] in Nothnagel's Clinic, Vienna, analyzed 206 cases of multiple sclerosis and found 5 cases occurring in lead workers. In 2, the symptoms and signs of the disease followed directly an attack of lead colic. Another patient gave a history of colic eight years before the onset. The other 2 workers gave no history of colic or of other usual evidences of lead poisoning. Hermann Eichhorst [11] also reported a typical case of multiple sclerosis

8. Marie, Pierre, referred to by Russell, Risien: Disseminated Sclerosis, in Allbutt, T. C., and Rolleston, H. D.: System of Medicine, ed. 2, New York, The Macmillan Company, 1910, vol. 7, p. 840.

9. Putnam, J. J.: On Certain Unrecognized Forms of Lead Poisoning, and on the Possibility of Mistaking Bismuth for Lead in Urine Analyses, Boston M. & S. J. **109**:315, 1883; Lead Poisoning Simulating Other Diseases, J. Nerv. & Ment. Dis. **10**:466, 1883.

10. Berger, A.: Eine Statistik über 206 Fälle von multipler Sklerose, Jahrb. f. Psychiat. u. Neurol. **25**:168, 1905.

11. Eichhorst, Hermann: Bleivergiftung und Rückenmarkskrankheiten, Med. Klin. **9**:201, 1913.

in a lead worker, with autopsy observations. Although the suggestion that lead might be an etiologic factor in multiple sclerosis has been revived many times, it has not been accepted.

Barker [12] dismissed poisoning by metallic substances such as lead on a series of counts. First, multiple sclerosis is probably as common in women as it is in men, and women are not, he thought, exposed as extensively to metallic poisons as men are. Second, the disease usually begins in early life, often at a period before the patients could have been subjected to metallic poisonings from occupations. Third, he stated that it is scarcely conceivable that the successive exacerbations that are characteristic of the disease can be explained on the ground of a succession of metal poisonings. Finally, in none of his series of 44 cases was there a history of metal poisoning.

The answer to Barker's pertinent points can be met on theoretical grounds from a study of the recent literature on lead poisoning. Meeting his objections will serve to show the state of knowledge concerning lead at the time the present investigation was begun. His first and second objections can be considered together. The reports of Park and his colleagues,[13] of Baltimore, and of Vogt,[14] of Boston, pointed out the frequency of lead poisoning in children. It has been conclusively shown that lead is stored in the growing ends of long bones and is present in such concentration that it casts a roentgen shadow, which is so characteristic as to make it diagnostic. Hitherto unsuspected cases in children have been discovered through roentgenographic examination. The number of children with lead poisoning, either occult or obvious, must greatly overshadow the number of adults with this condition due to industrial exposure.

The answer to the last objection is contained in the work of Aub, Fairhall, Minot and Reznikoff,[1] which shows how lead once stored may enter the blood stream again in response to a reaction of the body that liberates calcium. In this way, the succession of metal poisonings which Barker thought are scarcely conceivable can occur.

Storage of lead may take place without having at the time of its ingestion caused toxic signs. In such cases nothing may be obtained in the history suggesting metal poisoning; even close questioning may fail to bring out the history, because it either occurred in early life or

12. Barker, Lewellys F.: Exogenous Causes of Multiple Sclerosis, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1922, vol. 2, p. 22.

13. Park, E. A.; Jackson, D., and Kajdi, L.: Shadows Produced by Lead in X-Ray Pictures of Growing Skeleton, Am. J. Dis. Child. **41**:485 (March) 1931.

14. Vogt, E. C.: Roentgen Sign of Plumbism: Lead Line in Growing Bone, Am. J. Roentgenol. **24**:550 (Nov.) 1930; Roentgenologic Diagnosis of Lead Poisoning in Infants and Children, J. A. M. A. **98**:125 (Jan. 9) 1932.

escaped notice. Kehoe and others [15] have shown that the presence of small quantities of lead in the excreta of adults who have had no known exposure to lead is so common that it is, in itself, of no diagnostic value. When lead is found in the urine it means that it has come from the blood stream. Since so many persons show lead in the urine, absorption of lead into the body must be very common.

Any morbid agent which is suspected as the etiologic factor in multiple sclerosis must have a specific action on myelin. Demyelinization is the primary pathologic process in this disease. The fat granule cells arise as a result of destruction of myelin. Neuroglial scars follow the degeneration. In the changes in the blood vessels there is nothing specific, and they, too, must be secondary changes.

Lead has, for many years, been known to produce changes in the myelin of the peripheral nerves. Lancereaux,[16] in 1862, first pointed this out. Gombault,[17] in 1873, confirmed this observation and spoke of it as periaxial neuritis, since the axis-cylinders were not involved. Von Monakow,[18] Déjerine-Klumpke [19] and Doinikow [20] later described the histologic changes, and pointed out the patchy discontinuous degeneration of myelin. It was at first considered that no secondary degenerations occurred, but Doinikow showed that when the process was advanced destruction of nerve fibers took place, and wallerian degeneration occurred. The demyelinizing action of lead in the peripheral nerves of animals and man has been proved. In the central nervous system the descriptions are not clearcut. Von Monakow [18] described degenerated areas in the gray and white matter of the spinal cord in a case of lead poisoning. There were also scattered plaques of glial scarring in the tracts at various levels. Eichhorst reported the typical pathologic changes of multiple sclerosis in a lead worker. Though much experimental work on lead poisoning has been reported, we have been unable to find, in reviewing it, any description of involvement of myelin centrally such as occurs peripherally.

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15. Kehoe, R. A.; Edgar, G.; Thamann, F., and Saunders, L.: The Excretion of Lead by Normal Persons, J. A. M. A. **87**:2081 (Dec. 18) 1926.

16. Lancereaux, E.: Note rélative à un cas de paralysie saturnine avec altération des cordon nerveux et des muscles paralysés, Gaz. Méd. Paris **17**:709, 1862.

17. Gombault, M.: Contribution à l'étude anatomique de la névrite parenchymateuse subaiguë et chronique. Névrite segmentaire péri-axile, Arch. de neurol. **1**:11 and 177, 1880-1881.

18. von Monakow, C.: Zur pathologischen Anatomie der Bleilähmung und der saturninen Encephalopathie, Arch. f. Psychiat. **10**:495, 1880.

19. Déjerine-Klumpke, A.: Contribution à l'étude des polynévrites en général et des paralysies et atrophies saturnines en particulier, Paris, Félix Alcan, 1889.

20. Doinikow, B.: Beiträge zur Histologie und Histopathologie des peripheren Nerven, in Nissl, Franz, and Alzheimer, Alois: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1911, vol. 4, p. 445.

Dawson [21] and Hassin [22] concluded from their studies that multiple sclerosis is not due to the presence of a bacterial agent acting in the central nervous system. It is interesting to quote directly from both of these workers.

Hassin said in part:

> The essential feature of multiple sclerosis is a degeneration of the myelin. What causes this degeneration I do not know. It is certainly not an organism. Studies of the spinal fluid will bring out not only what multiple sclerosis is but also how to diagnose it scientifically and how to treat it.

Dawson [21] concluded from his extensive and careful studies of multiple sclerosis that:

> (i) The process underlying disseminated sclerosis is a subacute disseminated encephalomyelitis, which terminates in disseminated areas of actual and complete sclerosis. . . .
>
> It is probable that when the causal agent diffuses through the blood-vessel walls with average concentration and intensity, areas arise on the basis of . . . a primary solution of the myelin. . . .
>
> (ii) Disseminated sclerosis is probably not due to a developmental processes. . . .
>
> (iii) . . . there is much to favour the view that true disseminated sclerosis is due to a specific morbid agent which calls forth a clearly defined clinical and anatomical picture: . . . other disseminated affections of the central nervous system, such as disseminated arterio-sclerotic, syphilitic endarteritic, and acute encephalo-myelitic processes may all produce a symptom-complex very similar to that of disseminated sclerosis, but that they, in their further course, differ from the latter in the characteristic remissions and relapses, . . . acute infective diseases, trauma, chill, shock, and all known exogenous factors may act as exciting factors in lowering the resistance of the organism, and thus allowing the final determining factor to operate.
>
> (iv) The causal agent is, therefore, probably of the nature of a soluble toxin, and it is conveyed to the nervous tissues by the blood channel.
>
> (v) It is suggested, however, that the restriction and distribution of the pathological process is in some way related to the selective action of the toxin on certain areas of the blood supply, or that unknown factors determine an irregularly distributed paralytic dilatation, with an increased filtration through the vessel walls.
>
> (vi) The remissions and relapses, therefore, necessitate the assumption of the latent presence of the morbid agent in the body, or, if this is an autogenous toxin, either its intermittent evolution, or its accumulation from deficient elimination.

This "unknown morbid agent" postulated by Dawson, we think, could very well be lead.

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21. Dawson, James W.: The Histology of Disseminated Sclerosis, Rev. Neurol. & Psychiat. **14**:285, 337 and 541, 1916; **15**:47 and 369, 1917; **16**:287, 1918.

22. Hassin, George B.: Pathological Studies in the Pathogenesis of Multiple Sclerosis, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1922, vol. 2, p. 144.

In reviving lead as a possible cause of multiple sclerosis we have the advantage over former observers, owing to the improvements in the methods of chemical examinations and the recent studies of the physiologic behavior of lead in the organism. Eichhorst [11] suspected lead strongly as a cause of multiple sclerosis and other allied organic lesions of the central nervous system, but had no method of proving it. Lead in the excreta was not entirely convincing, and the fact that a man had been exposed to lead did not exclude the possibility of a quite unrelated organic disease.

We can now see better the similarity in the process of demyelinization in both nerves and cord in lead poisoning and multiple sclerosis. We now appreciate sources of poisoning never before considered. We now realize the potentialities of ingested lead which has become stored in the bones. We can now prove the presence of lead, at least qualitatively, in the spinal fluid.

We appreciate that the question will not be finally answered until we can produce multiple sclerosis by the experimental ingestion of lead. If appropriate therapy causes lead to disappear from the spinal fluid and prevents exacerbations, this fact will aid.

SUMMARY

1. Lead has been found in the spinal cord at necropsy in 1 typical case of multiple sclerosis.

In a case of neuromyelitis optica, lead was present in the brain and the spinal cord. The brain, which showed areas of loss of myelin and scarring, contained larger amounts of lead than the normal-appearing brain. The spinal cord with its marked involvement showed more lead than the normal-appearing brain stem.

2. Six cases of multiple sclerosis of the type progressing by exacerbation and undergoing remissions have shown lead in the stools, urine and cerebrospinal fluid. In 3 cases studied at some length, lead increased in the excreta during acidosis and diminished greatly under calcium therapy.

3. The value of calcium therapy was shown in the patient with neuromyelitis optica. Calcium stopped the advancing myelitis and caused lead to disappear from the spinal fluid. It is too early for us to state whether or not calcium is a satisfactory therapeutic agent in multiple sclerosis.

4. We cannot state dogmatically that because lead is found in the central nervous system, in the spinal fluid, in the bones and liver and in the excreta, it is therefore the cause of the disease. The constant association, however, of lead in every case of multiple sclerosis of the type under discussion that we have studied builds a rather strong incrim-

inating argument, provided we have not overlooked some fault in methods and have not interpreted our findings wrongly.

5. More evidence may be brought to bear on the subject by experimental work now under way, by further study of cases and by investigations in other clinics which we hope this report will stimulate.

6. Our work to date certainly suggests lead as the possible etiologic agent in multiple sclerosis of the exacerbating and remitting type.

DISCUSSION

Dr. J. C. Aub, Boston: I cannot discuss with any degree of authority the neurologic side, but I should like to say a few words about the effect of heavy metals such as lead, their excretion and their appearance in life in general. Lead is apparently present in a very large percentage of normal persons. At the time of our studies we did not find this, owing, no doubt, to the fact that we analyzed as normal persons those who worked in laboratories and were therefore greatly protected. However, it is only fair to say that all investigators since that time, that is, in the last six years, have found excretion of lead in normal persons. The reason for this is obvious. The dust on the streets must contain a good deal of lead, and it is present in rubber tires, in ethyl gasoline and in other agents to which one is exposed. The result is that minimal quantities of lead may be found in every one.

In medicine, the problem always arises as to whether the lead is a normal constituent, that is, due to absorption, or whether it is really causing toxic effects. This is always a difficult problem to answer, but it seems fair to say that if lead is causing any obvious abnormalities in the tissues of the body, then it is an intoxication. The most likely place for discovering this is in the blood. The reason why study of the blood is so important is that if lead is circulating in the body it always produces an effect on the red blood cells, which are primarily exposed and are very susceptible to lead, thereby causing secondary anemia and characteristic stippling.

As previously stated, an excretion of lead can be found in many normal people. Therefore, it is difficult to determine whether the very marked effect of an acid diet, as shown in a slide, is definitely abnormal. It seems to me that it is, but I should not like to be categorical about it.

Lead is stored in the bones. While it is in the bones, as Dr. Russel has said, it is quite inert. When it is liberated from the bones and is circulating in the organism, it causes toxic effects. Therefore, lead is found in fairly high concentration in tissues when death is caused by it. If further work is done, I should like to stress the importance of analyzing tissues other than those of the brain. The most important organ is the liver because it absorbs and retains high concentrations of the lead which is circulating in the body, and would therefore be of great assistance in the final determination of the importance of lead in any disease of the central nervous system.

Dr. Henry Alsop Riley, New York: An investigation of this kind is of extreme importance, and too great praise cannot be expressed concerning the very exact technic with which the estimations of the various metals were made and the manner in which the material was handled. It seems to me, however, that any effort to determine any one particular toxic factor as productive of the disease which is called multiple sclerosis must be most rigidly examined. The choice of

clinical cases as examples of the disease must be controlled by the most rigid criteria, and most careful estimation of the clinical histories must be carried out in order to include in the group only those patients who would be accepted by an overwhelming proportion of neurologists as suffering from multiple sclerosis.

I hesitate to express my own doubt in regard to some of the cases which Dr. Russel and his associates have chosen for this investigation because he himself has said that they were cases of typical multiple sclerosis. It seems to me that some of the cases are somewhat open to question as to the clinical diagnosis of multiple sclerosis. Time does not permit me to give in full my reasons for questioning the clinical diagnosis. The first case to which he referred, that of the patient suffering from a retrobulbar neuritis, would certainly seem to be one of lead intoxication with a very considerable degree of saturation with the metal, presenting evidence of involvement of the optic nerve, the brain and the spinal cord due to this specific intoxicant and not a case of multiple sclerosis.

The second case was primarily an acute condition developing in the course of pregnancy and presenting disturbances of the pyramidal tract, sphincteric disorders and sensory alterations. Whether this case is quite admissible to a group of cases of multiple sclerosis, considering the complication brought about by the pregnant state, I am not sure.

Among the cases which make up the body of Dr. Russel's investigation, I think that case 3 would be accepted by every one as a case of typical multiple sclerosis from the history and results of physical examination. Considerable emphasis was placed on the patient's occupation as a dry-goods merchant who spent a great deal of time sucking a pencil and moistening his samples with his tongue. Whether these habits can be considered as a sufficient source for lead intoxication is a matter for those who are more experienced than I am in determining the amount of lead which can be absorbed from such sources.

The fourth case was a typical case of multiple sclerosis but of rather short duration and not showing any definite history of remission, and there is the possibility in this instance of the presence of a dorsolateral sclerosis.

Case 5 appeared to me as being in essence a toxic encephalomyelopathy, and it seemed to me that the history was typical of a situation consisting in great part of a multiple neuritis followed by the development of a myelopathy.

I should have some hesitation in accepting case 7 as one typical of multiple sclerosis. The patient in case 8 was suffering, without doubt, from multiple sclerosis.

Among the control cases which Dr. Russel reports, 2 were of the typical progressive remitting type of multiple sclerosis. Neither of these cases showed any lead.

It seems to me, without question, that in some of the cases reported the patients were suffering from multiple sclerosis, and that in others the patients presented widespread evidences of neural intoxication exemplified by neuropathies, myelopathies and encephalopathies.

It is rather difficult to divide the clinical entity of multiple sclerosis into two types that are similar in character but differ in the extremely important feature of the presence of lead in varying quantities in one group and its absence in the other and still consider them both typical of the disease multiple sclerosis.

Patients with lead in their systems are apparently for some obscure reason subject to waves of liberation of lead resulting in exacerbations of the symptoms, contrasting with quiescent periods in which the lead is relatively fixed and in which there are no particular progressive symptoms. Are these periods of recrudescent symptoms due to the liberation of the lead and its intoxicating

effect on the nervous system through the blood stream the same phenomena as those observed in the disease recognized as multiple sclerosis?

I took the opportunity of reviewing about 50 cases of clinically diagnosed multiple sclerosis at the Neurological Institute, and in them, as is emphasized by Professor Aub, I looked for changes in other tissues, particularly those of the blood. Among the 50 cases, there were only 3 which showed a secondary anemia, and in no instance was stippling of the red blood cells mentioned.

The changes in the spinal fluid are perhaps not admissible criteria on account of the fact that any myelopathy, whether from toxic, metabolic, lipolytic or unknown causes, may show changes in the total protein content of the spinal fluid and the globulin. In only 3 cases were the excreta examined for lead; in 1 instance the stool was examined, and was negative for lead; in the other 2 instances, specimens of urine were examined, and in 1 case 0.11 mg. was found, while in the other 0.07 mg. was found.

As a result of these considerations I feel that while our approval and encouragement should be given to every effort to determine the cause of multiple sclerosis, one should be rigidly conservative in the choice of clinical material and accept only cases which from 90 to 95 or perhaps 100 per cent of neurologists would accept as cases of multiple sclerosis. The final result of the determination of a possible metallic intoxicant should not be challenged by any questions as to the absolutely typical character of the clinical material.

I believe that this study should receive confirmation or refutation, and I hope that it will result in the careful investigation of possible metallic intoxicants in patients suffering from multiple sclerosis in other centers of neurologic activity. Certainly from the evidence which I have shown, very little attention was paid at the Neurological Institute to the determination of these heavy metals as causative factors in the production of this symptom picture. If it does nothing else but draw attention to the necessity for these investigations, I believe that the contribution is fully justified.

DR. RICHARD M. BRICKNER, New York: I wish to emphasize the note of caution sounded by Dr. Aub and Dr. Riley. I have worked in the field of multiple sclerosis for five years and am keenly aware of the difficulties involved in making any evaluations that are connected with the disease, because of the several pitfalls that investigators are likely to meet when they study multiple sclerosis. In our investigation we have had from 125 to 150 cases. All of these cases, or practically all, have been diagnosed and agreed on as cases of multiple sclerosis by all of the observers who saw them. Even so, some time ago I made up my mind and published the statement that perhaps 20 per cent of the cases may not be cases of multiple sclerosis. I think that it is almost impossible to be entirely sure of what one is doing scientifically when there is no basis but clinical observation and reasoning on which to select material.

This, of course, is not a reason for refraining from investigating the disease. It is merely a reason for being particularly cautious.

Another indication for caution is this: It is curious that in the last five years or so no less than six different causes of multiple sclerosis have been suggested. One of them was promulgated earlier than the rest; this was Steiner's spirochete. Purves-Stewart and his spherula are known to all; there were also Putnam's work on tetanus toxin and Ferraro's work with potassium cyanide, in both of which demyelinization was produced by the toxin; my work on the lipases suggested, after an idea given by Marburg some years ago, that abnormal lipase activity might be responsible for the lesions, and most recently Löwenstein found tubercle bacilli, I believe, in 42 per cent of the cases of multiple sclerosis he studied.

There is a melange of causes; one of them may be right, none of them may be right, or they may all be right. In this connection, it must be remembered that the condition called multiple sclerosis may really be an aggregation of several conditions which resemble each other clinically, but which have different causes. It may be that the present students will be able to delimit such a group.

I should like to repeat one statement which I have made before, and it applies to my own work as rigidly as it does to that of any one else. I do not believe that any one should say that he has found the cause of multiple sclerosis until he has been able to reproduce the disease or something very similar to it with materials that have been obtained from the bodies of patients.

Of course, it is known that every patient with lead poisoning does not have multiple sclerosis or anything comparable to it. It may be that, in order to develop multiple sclerosis from lead poisoning, some at present unknown form of sensitivity must be present. Hence, the present authors may be right and still be unable to reproduce the disease in animals with lead because there is no such sensitivity. Nevertheless, before lead poisoning is finally accepted as a cause, every effort should be made to reproduce a similar condition with lead in animals.

Dr. Smith Ely Jelliffe, New York: One of the sad things of living fifty or sixty years is to see the masses of unfulfilled hopes and wishes, in the form of papers, monographs and so forth, that accumulate as a result of one's interests. For forty years multiple sclerosis has been one of mine. I have manuscripts of notes and histories and discussions on multiple sclerosis, 20 or 30 pounds of them, starting with a monograph that I was going to write before 1904, when Müller's celebrated monograph appeared and more or less cut the ground from under my feet because of its rich accumulation of pathologic material which I did not have.

From time to time this society has listened to discussions about so-called multiple sclerosis, and every time it is talked about as a disease per se I boil. I am prepared to froth at the mouth when one talks of typical multiple sclerosis. Even with such a clearcut entity as "pneumonia," who talks about typical pneumonia at the present time? Are there not types A, B, C, D and so on? When one talks about typical multiple sclerosis, what is one talking about? One is not talking about anything at all. There is no such thing as typical multiple sclerosis unless one would arbitrarily erect an artefact that does not exist except as an abstraction.

We have just listened to an excellent description of multiple sclerosis caused by lead, if you will. Marie, as we all know, described and discussed in the early part of the century multiple scleroses following measles, multiple sclerosis following scarlet fever, multiple sclerosis following whooping cough, and practically all of the infectious diseases were in a few isolated cases followed by irregular "multiple scleroses."

Since the epidemic of encephalitis, there have been a good many types of so-called multiple sclerosis: arsenical multiple sclerosis, syphilitic multiple sclerosis and even Jelliffe's psychogenic multiple sclerosis.

So possibly I may add, following Dr. Brickner's last remark, that all one has to do is to take a patient with almost psychogenic multiple sclerosis and dose him with lead, and one can produce "typical multiple sclerosis."

Where are we going to come out if we talk about a series of differently induced processes as a disease per se? The interesting point is, what are the metabolic disturbances which tend to produce certain kinds of deterioration and

degeneration in certain of the elements of the nervous system? And, further, how, by a complex series of interlocking dynamic processes—more intricate than any of the economic ones with which we have been afflicted in recent years—do certain irreversible processes take place in the spinal cord and brain which result in a motley group of encephalomyelopathies, which may be roughly thrown into nosological affiliation and given a name? As Hobbes reminded us: "Words are but counters, and wise men do but reckon with them."

Dr. Foster Kennedy, New York: I believe that Dr. Russel has in mind a perfectly definite picture which he calls multiple sclerosis, and that he is referring to that picture of disease which occurs within very definite age limits, rarely appearing after 40 or before 18 or 16, and confined to—not confined to but very much emphasized in—the nonpigmented people, the less pigmented people, light-haired and blue-eyed people. I wonder how Dr. Russel will be able to unite the idea that these people in a definite period of life and with definite congenital characteristics become more liable to lead poisoning than others.

I should think that if multiple sclerosis, as Dr. Russel understands it, were due to chronic lead poisoning or acute lead poisoning, it would be seen more in older people and less in younger people.

Dr. Arthur Weil, Chicago: We know that there is a tremendous overgrowth in the plaques not only of fibrous glia but of microglia as well. The latter has excellent storage facilities for inorganic compounds.

I am reminded of dementia paralytica in which inorganic iron is found in large amounts within the rod cells. No one, however, believes that this increase in inorganic iron is a cause of dementia paralytica. It may well be possible that an increased amount of lead in the organism causes the microglia within the plaques to accumulate lead, and therefore this accumulation may be found in the brain and spinal cord of patients with disseminated sclerosis.

Did Dr. Russel and his co-workers consider this fact? I think that the point can easily be settled if they can demonstrate the same amount of lead in the central nervous system of patients with disseminated sclerosis living in the northern forests, in places far away from the lead-contaminated air and water of the large cities.

Dr. William V. Cone, Montreal, Canada: It is difficult to comment on all of the points that have arisen in the discussion. I shall try to state our ideas regarding them.

Dr. Aub has spoken about the presence of lead in the blood stream and its effect on the red blood cells. We have studied the blood in these patients with the spectrograph and have been able to demonstrate three lead lines in the spectrum in most of them. We have also studied the blood of normal persons, or apparently normal persons, spectrographically, and have also found one or two lead lines in these supposedly normal subjects. We do not know the significance of this.

Stippling of the red blood cells in our cases has been an evanescent thing. For example, we have found stippled red cells, and then in a smear made one hour later we have not been able to find them, though in subsequent spreads they have been found again. Why this variability occurs, I do not know.

Regarding the possible source of lead in our cases, we must point out that in many of them it was not clear. Recently, however, we have seen in Montreal a considerable number of cases of lead poisoning in children. The work of Vogt and Parks, which pointed out that lead is stored in the epiphyseal lines of growing bones, has made the diagnosis easy by roentgenograms. Our patients are, of course, past the age at which epiphyseal lines occur. It has been our

belief that our patients may have ingested lead in early life and that it was stored in the skeleton, from which it can be liberated at any time when the metabolism changes.

A few of the patients have had a rather definite history of exposure to lead. Dr. Riley spoke of the patient who licked his lead pencil. I have been informed that the larger firms in America now use lacquer paints free from lead. Some of the pencils imported from Germany are said to have lead paint on them. The particular patient he referred to, we believe, obtained most of his lead from leaded silk. He was in the dry-goods business, and it was his custom to test the color fastness of silks by putting them in his mouth and licking them. He said that he did this hundreds of times a day and had begun it at the age of 12. He was 16 when the first signs of multiple sclerosis appeared. He brought us several samples of silk. That which he said was heavily leaded cast a shadow under the fluoroscope; the silk not leaded cast no shadow.

Dr. Riley has raised the question as to whether these cases are really cases of multiple sclerosis. In practically every case in this series the diagnosis of multiple sclerosis was made in other clinics before we saw them. We believe that they are typical cases. In the patient he referred to in whom the onset of symptoms occurred during pregnancy, it is interesting, in support of our hypothesis, to mention the waves of progression which occurred with pregnancy. During the first pregnancy pain in the right leg and paresthesia developed. These complaints lasted but a few days and then stopped entirely. During the second pregnancy one year later the difficulty began again in the right leg and advanced. With the third pregnancy, there was a marked accentuation of signs, the left leg was involved, both legs became spastic, and sphincteric disturbances were extreme. In this patient three striking episodes occurred, and they took place in each instance during either pregnancy or lactation. Lactation and pregnancy can produce striking disturbances in calcium metabolism and cause calcium to be given up from the skeleton. If lead has been stored, it will be liberated with the calcium.

We have demonstrated lead in the spinal fluid in 11 patients who did not have multiple sclerosis. These cases are more characteristic of well recognized lead poisoning and showed the neurologic signs one sees in children with proved lead intoxication. We hope to make these the subject of a future report.

We studied the spinal fluid repeatedly in 20 patients suffering from a variety of neurologic conditions and found no lead. They serve as our control series. One question does arise, however, which worries us. If lead is circulating in the blood stream as we have found it to be in a so-called normal person, might there be periods in which the meningeal permeability and that of the choroid plexus could be altered so that lead might get through and not be significant of involvement of the central nervous system with lead? I believe, for example, that arsenic has been demonstrated in the spinal fluid after its intravenous injection and lumbar puncture.

It is obvious that we have placed a great deal of weight on the Fairhall hexanitrite test. We have found no flaws in it when it is rigidly controlled so that contamination is ruled out. Dr. Fairhall has checked our procedure and has been good enough to verify our findings in 1 case, that of the dry-goods merchant. We demonstrated hexanitrite crystals in the spinal fluid on seven different occasions before a specimen was sent to Dr. Fairhall.

Some of the cases in adults in which we have found lead in the spinal fluid have been typical cases of lead encephalopathy and myelopathy such as Dr. Kennedy has mentioned. We are all familiar with this type of lead poisoning.

It is relatively easy to reproduce the conditions in animals at will by acute and subacute intoxications.

We hope to be able by subminimal doses of lead to produce a more chronic type of change in animals so that only the demyelinizing action of lead takes place, and the mesodermal and meningitic reaction is avoided. The literature is full of descriptions of experimental lesions of the central nervous system in acute and subacute intoxications, but contains little on the very chronic types.

I shall not attempt to answer Dr. Jelliffe, for I know so little about the psychogenetic phase of the problem.

Dr. Brickner's points are very pertinent. We will welcome any cooperation we can arrange because we believe that the problem is very important, and do not want to go astray. We have a patient in our series who was treated with the so-called specific serum for multiple sclerosis which was used by Sir James Purves-Stewart until quite recently.

Dr. Colin K. Russel, Montreal, Canada: Dr. Cone has answered most of the questions that have been asked. But it occurs to me that the multiple sclerosis that has been described as following acute infections might very well be explained by the known action of acute infections in changing the hydrogen ion concentration of the blood, thereby mobilizing the lead and thus repoisoning the patient. All of these acute infections have been blamed by various authors at various times as etiologic factors in multiple sclerosis; in the same way pregnancy has been blamed. Gowers reported such cases, and the obvious demand of the fetus on the calcium supply of the mother would naturally mobilize the lead with the calcium and thus cause repoisoning.

I am not a chemist, and I am afraid that I am not capable of discussing Dr. Brickner's point about the disturbances in the lipases, but I wonder whether the well known action of lead in causing stippling in red blood cells and its action as a demyelinizing agent would not also explain the lipoid disturbance.

As for lead as a cause of multiple sclerosis, this is not a new idea. It has been suggested many times by many workers. Eichhorst, in 1913, for instance, reported several cases, one a typical case of multiple sclerosis with autopsy observations. He repeatedly suggested that he thought that lead might very well be the cause, but the methods at his disposal in those days were not sufficient to prove the case, to justify that suggestion. The mere fact of lead in the excreta was not sufficient, and the fact that the patient had been a lead worker did not exclude other organic diseases altogether unrelated to lead. We appreciate that fact.

With regard to Foster Kennedy's question, we believe that lead poisoning or lead ingested in infancy and childhood is a much more important factor even than industrial lead poisoning. We believe that the lead may very likely be stored in the bones for many years. Such cases have been reported. Yet it becomes mobilized with a change in the hydrogen ion concentration.

MULTIPLE SCLEROSIS AND AMYOTROPHIES

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Multiple sclerosis is well defined clinically by signs and symptoms referable to almost any part of the central nervous system. Pathologically, it is characterized by numerous plaques scattered throughout the neural axis and involving essentially the white matter. The main feature of the plaque is the destruction of the myelin sheaths, with some sparing of the axis-cylinders and ganglion cells, and a replacement of the destroyed parenchyma by an excessive increase in glia. Occasionally cases of this protean disease are encountered which do not conform to the classic description and which offer diagnostic difficulties, such as those marked by the atrophy of muscles. Of a series of 20 cases of multiple sclerosis which came to necropsy, 12 showed atrophy of one or more groups of muscles or of a whole extremity; atrophies of this nature also occurred in 17 of 110 other cases of multiple sclerosis observed clinically at Montefiore Hospital since 1923. Pathologically, in addition to destruction of the white matter, plaques implicating the gray matter of the spinal cord and destroying the anterior horn cells accounted for the atrophies. Although such atrophies have been occasionally described, they were found in such a large number of our patients that they merit more emphasis and study than they have hitherto received.

The first case will be described in detail; the others will be summarized briefly.

The spinal cords of these patients were sectioned transversely and were stained by the myelin sheath, cresyl violet, Bielschowsky, victoria blue and sudan IV methods.

REPORT OF CASES

CASE 1.—A. S., a married woman, aged 45, was admitted to the hospital on Jan. 5, 1931, with a history of sudden blindness when she was 29 years of age. This had lasted for thirteen weeks. Subsequent to this she had transient attacks

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of hemiplegia, one at the age of 30 and another at the age of 36. When she was 38, she experienced weakness of the lower extremities; this progressed until she was finally confined to a wheel chair. She had been incontinent of urine and feces for one year prior to admission.

Neurologic Examination.—This revealed: pupils sluggish to light; primary left optic atrophy; cerebellar signs in the left upper extremities and spontaneous involuntary flexion movements of the lower extremities; diminished power in the upper extremities; general atrophy of all the muscles, which was most marked in the intrinsic muscles of the hand; absence of the knee and ankle jerks on the left; a bilateral Babinski reflex and allied signs; hypalgesia below the sixth dorsal segment

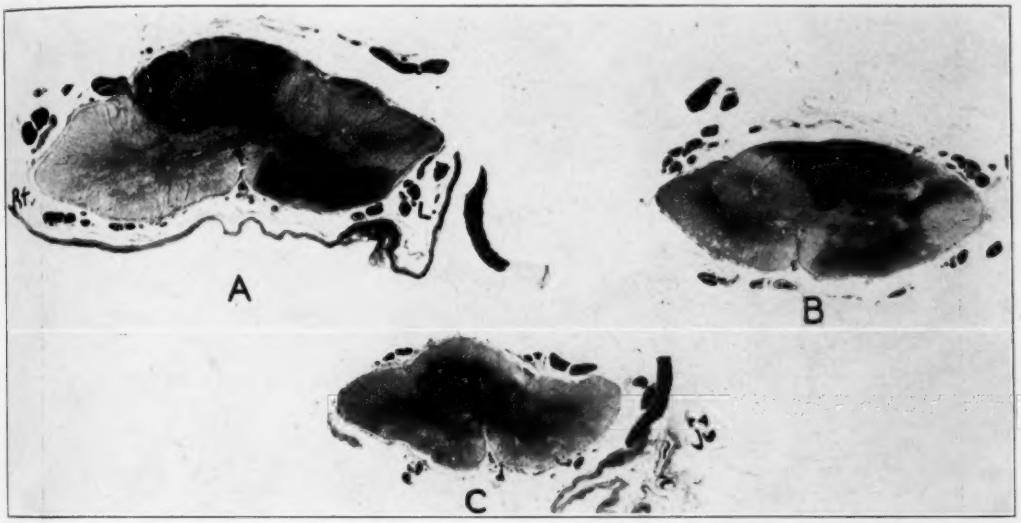

Fig. 1 (case 1).—*A*, section from the cervical region showing a plaque involving the lateral pyramidal, cerebellar and spinothalamic pathways on each side of the cord and the gray matter on the right side. The left anterior pyramidal and ventrospinothalamic tracts were less damaged, and the fasciculus gracilis disclosed only a slight ascending demyelinization. *B*, section through the lower cervical region showing plaques of the gray and white matter somewhat similar to those in *A*. *C*, section of the middorsal segment, disclosing almost complete demyelinization of all fiber tracts.

and loss of the sense of position in the toes, ankles and left knee; incontinence of urine and feces, and euphoria.

Laboratory data showed nothing significant except secondary anemia and the presence of albumin in the urine.

Outcome.—The patient died on January 19, following a severe urinary infection.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis and cystopyelonephritis.

Autopsy.—Gross Examination: There was atrophy of the convolutions of the brain; numerous old and fresh plaques were scattered throughout the white matter

of the cerebral hemispheres and in the gray masses of the diencephalic and mesencephalic nuclei. There was atrophy of the lower two thirds of the dorsal region of the spinal cord, and the outlines of the gray and white matter in these segments could not be distinguished.

Microscopic Examination: The sclerotic plaques of the white matter of the cerebral hemispheres and some of the subcortical gray masses disclosed the histopathologic changes usual in multiple sclerosis.

Sections from the cervical region of the spinal cord showed a plaque involving the lateral pyramidal, cerebellar and spinothalamic pathways on each side of the cord and the gray matter on the right side (fig. 1 *A*). The left anterior pyramidal

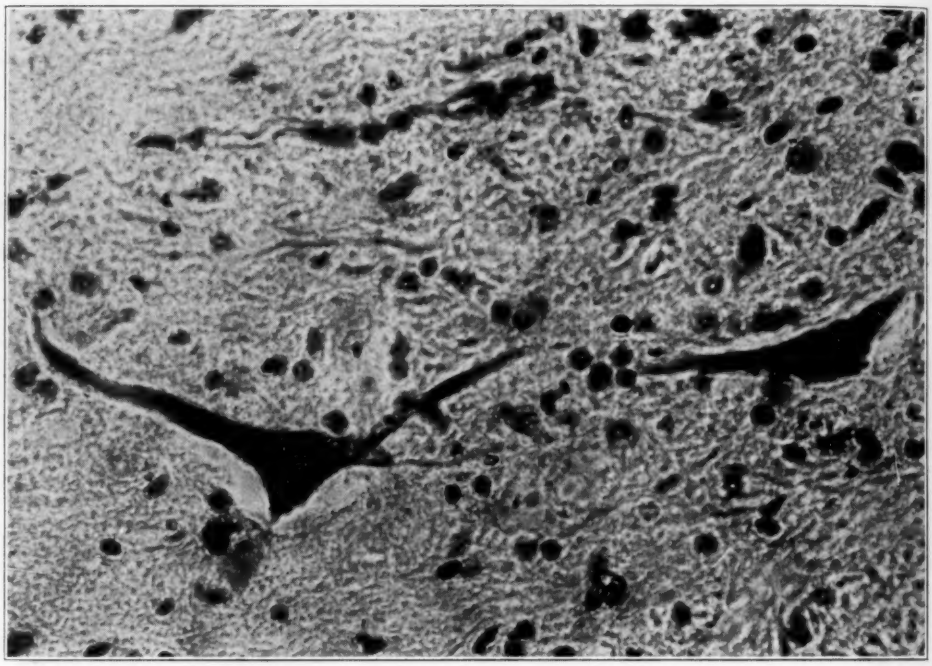

Fig. 2.—Sclerotic changes of anterior horn cells. Cresyl violet stain; × 500.

and ventral spinothalamic tracts were less damaged, and the fasciculus gracilis disclosed only a slight ascending demyelinization. In the sections stained with cresyl violet the anterior horn cells on the right were found to be decreased in number, shrunken and pyknotic and to have prolonged corkscrew processes; their nuclei could not be identified (sclerotic cell changes—fig. 2). Some of the nerve cells showed disintegration of the Nissl substance (fig. 3), with a tendency of the chromatin granules to form clumps and collect at the periphery (fig. 3).

In a section from the lower cervical region (fig. 1, *B*) the changes in the nerve cells were similar to those just described. There were, in addition, swollen ganglion cells, eccentric nuclei and loss of Nissl substance and processes. At the middorsal segment, except for part of the posterior columns, the cord was completely demyelinated (fig. 1, *C*). With a higher magnification a few of the

myelin sheaths which could still be identified were seen to be swollen and disintegrated. The anterior horn cells, although damaged and showing sclerotic changes, were better preserved at this level than in the cervical segments. The axis-cylinders in these sections were swollen and had ball-like terminations and corkscrew processes; some were well preserved. There was an increase in the glia fibers in the plaques of the white and gray matter of the cervical and dorsal regions.

Comment.—The atrophy of practically all the groups of muscles, which was most noticeable in the intrinsic muscles of the hand, was due to destruction of the

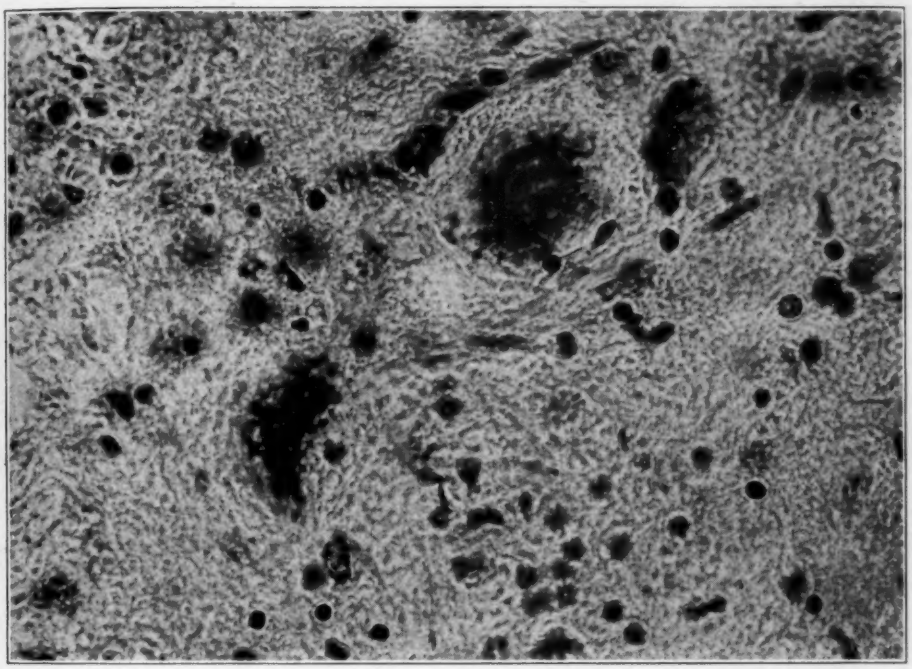

Fig. 3.—Disintegration of anterior horn cells, with a tendency of the chromatin granules to form clumps. Cresyl violet stain; × 500.

anterior horn cells by the plaques which had invaded the gray matter. The marked diminution in number, the disintegration and the sclerotic changes of the anterior horn cells (figs. 2 and 3) proved conclusively that we were not confronted with diseased cells due to axonal degeneration but with primary cellular changes as a result of implication of the gray matter.

CASE 2.—F. F., a woman, aged 58, was admitted to the hospital with a history of double vision when she was 38 years of age, weakness of both lower extremities five years later and occasional "shooting pain" in the face on exposure to cold. She had been confined to a wheel chair since the age of 45.

Neurologic examination disclosed: ptosis of the right upper eyelid; extensive involvement of the external ocular muscles, with loss of associated lateral move-

ments; lateral nystagmus; bilateral corneal hypesthesia; facial paralysis of the right central and left peripheral regions; diminished hearing on the left; deviation of the uvula to the left; atrophy of the left side of the tongue; dysarthria; flaccidity and atrophy of the muscles of both upper extremities, with complete paralysis of the right upper extremity; absence of deep reflexes on the right, with the exception of the ankle jerk; absence of the abdominal reflexes; a positive Babinski reflex and allied signs; hypesthesia and hypalgesia of the entire right side of the body; defective two-point discrimination throughout; dysstereognosis in the right hand

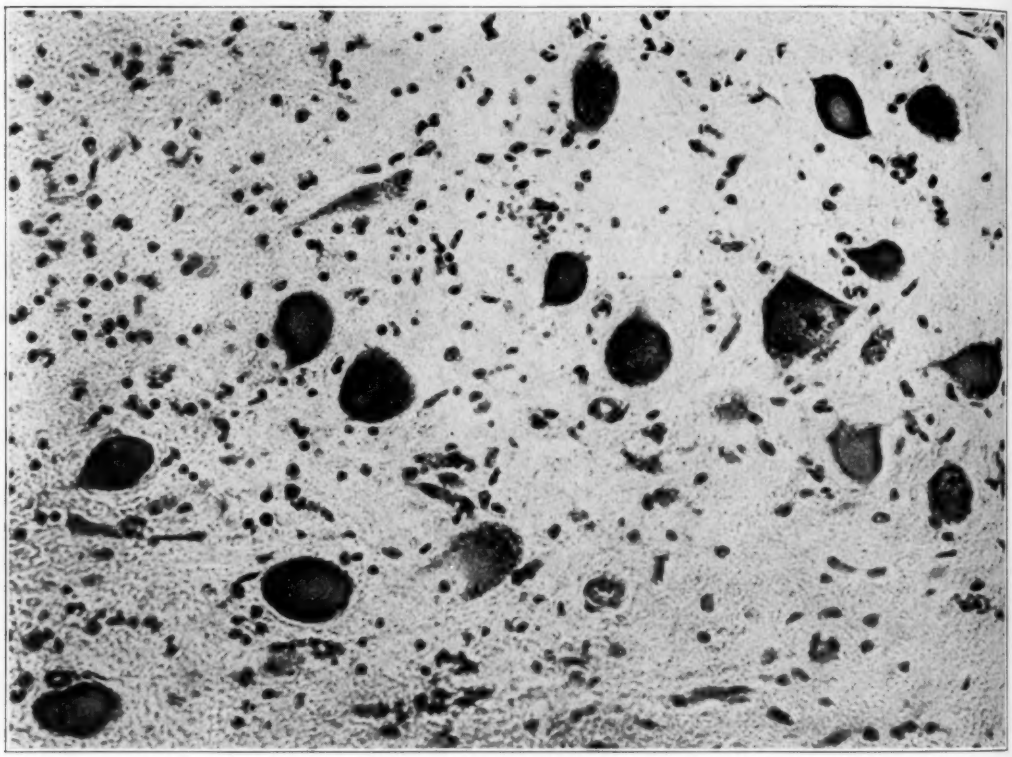

Fig. 4 (case 2).—Anterior horn cells of the anterolateral and anteromesial groups, showing axonal or retrograde degeneration. Cresyl violet stain; × 200.

and impaired vibratory sense in the right upper extremity and in both lower extremities.

Laboratory data showed nothing abnormal except a slight trace of albumin in the urine.

Course.—Six months after admission difficulty in breathing and pseudobulbar signs developed. Examination disclosed, in addition to the findings already mentioned, weakness of the right sternocleidomastoid and trapezius muscles, marked atrophy of the small and large muscles of the right upper extremity and slight atrophy of the small muscles of the left hand. The patient died of bronchopneumonia at the age of 61.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis and bronchopneumonia.

Autopsy.—Gross Examination: There was atrophy of the cortical convolutions and of the pons; all the ventricles were dilated; numerous fresh and old plaques were scattered throughout the white and gray matter of the hemispheres, midbrain and brain stem. The spinal cord was atrophic; transverse sections revealed plaques destroying the gray and white matter at various levels.

Microscopic Examination of the Spinal Cord: In the eighth cervical segment a plaque had destroyed the direct pyramidal, ventrocerebellar, rubrospinal and spinothalamic pathways, as well as the gray matter. At the seventh dorsal segment a plaque had destroyed the posterior columns, the left crossed pyramidal tract, a part of the dorsocerebellar pathway and some of the gray matter. In this region dense glia fibers had replaced most of the gray matter. Some of the anterior horn cells were destroyed; others showed pigmentary atrophy, sclerosis or complete disintegration; most, however, disclosed pathologic changes similar to those seen in retrograde degeneration (fig. 4). The anterolateral and anteromesial groups were more involved than the dorsolateral and dorsomesial groups.

Comment.—This patient presented marked atrophy of the muscles, with corresponding changes in the ganglion cells. The outstanding histopathologic picture was axonal degeneration (fig. 4).

CASE 3.—M. L., a woman, aged 39, was admitted to the hospital with a history of repeated transient attacks of weakness in the lower extremities since the age of 18, which had finally led to spasticity and had confined her to bed. Three years prior to death intention tremor of the upper extremities and frequency of urination had developed.

Neurologic Examination.—This revealed: pupils fixed to light; pallor of the left disk; nystagmus; bilateral corneal hypesthesia; atrophy of the intrinsic muscles of the hands; spastic paraplegia in flexion, with bilateral pyramidal tract signs; ataxia and intention tremor; scanning speech; parkinsonian pill-rolling tremor; rigidity of the right arm and leg; loss of the vibratory sense in the lower extremities and impairment of the sense of position in the toes; perseveration, palilalia and grimaces; severe apraxia; marked mental changes, with defect of memory, poor insight and marked confusion on very simple commands.

Laboratory data showed no abnormalities except a trace of albumin and occasional red blood cells in the urine.

Course.—A carcinoma developed in the left breast, with metastases, and the patient died at the age of 41.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis and carcinoma of the left breast with generalized metastases.

Autopsy.—Gross Examination: There was marked atrophy of the cerebral convolutions, with dilatation of the ventricular system; numerous plaques were scattered throughout the white and gray matter of the central nervous system. The lower dorsal region of the spinal cord was constricted. Transverse sections of the cord revealed plaques in many segments.

Microscopic Examination: In the spinal cord, plaques had destroyed most of the white and gray matter of the cervical and upper dorsal segments; the lower dorsal segments were less extensively involved; the anterior horn cells of the gray

matter showed various destructive changes: complete disappearance of the cells, homogeneity, chromatolysis and eccentric nuclei. Sclerotic cells, pigmentary atrophy and "shadow cells" were also observed. Many of the nerve cells showed accumulation of fat when stained with sudan IV (fig. 5). The destroyed gray matter had been replaced by dense glia fibers and cells.

Comment.—The atrophy of the intrinsic muscles of the hand was definitely due to changes in the anterior horn cells of the cervical segments. The marked involvement of the ganglion cells of the upper dorsal segments is of interest. It

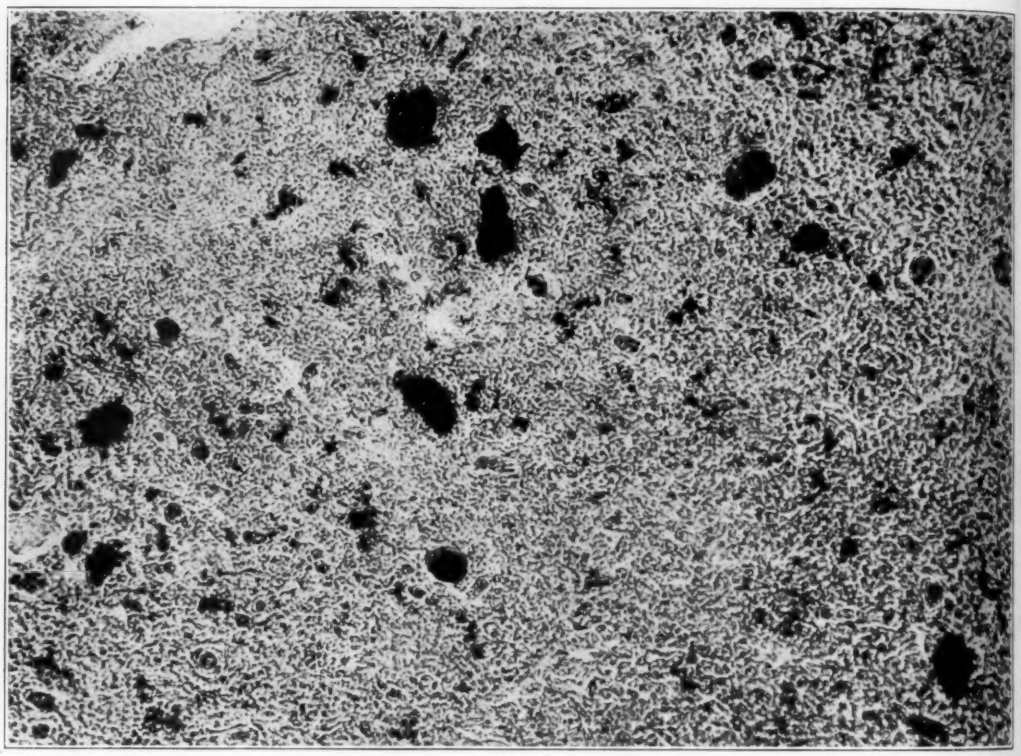

Fig. 5 (case 3).—Anterior horn cells, showing marked accumulation of fat. Sudan IV stain; × 200.

is, of course, possible that atrophy of the corresponding muscles of the trunk was present, but this was not noted by the examiners.

CASE 4.—M. P., a woman, aged 35, was admitted to the hospital with a history of a fall down a flight of stairs five years previously. A year later she dragged the lower extremities and had incontinence of urine.

Neurologic Examination.—This revealed: irregular pupils, the right being larger than the left; bitemporal pallor; nystagmus in all planes; deviation of the uvula to the left; atrophy of the interossei, the thenar and hypothenar eminences and the muscles of the lower extremities; bilateral pyramidal tract signs; diminished abdominal reflexes; bilateral intention tremor; left adiadokokinesis, and diminished sense of vibration in the lower extremities.

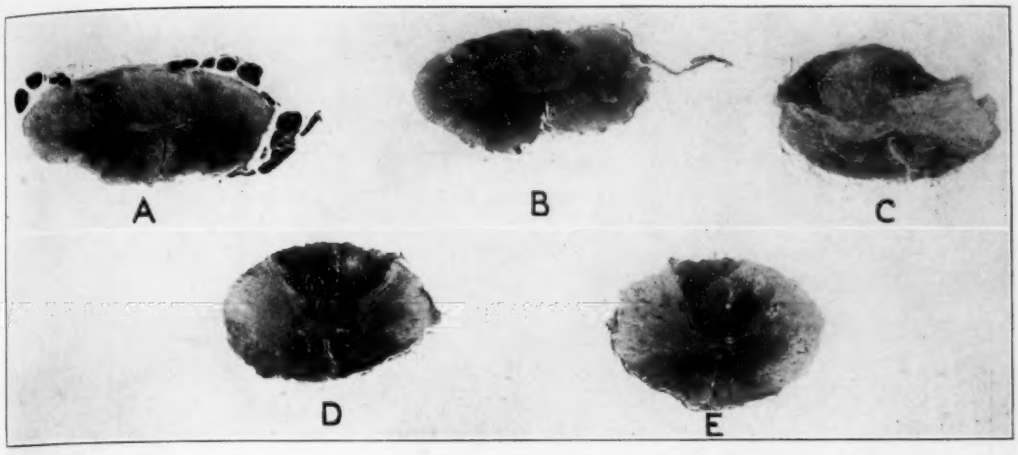

Fig. 6 (case 4).—*A* and *B*, plaques destroying most of the gray and white matter of the lower cervical segments. *C*, section of the upper dorsal segment, showing destruction of the columns of Goll and Burdach, the lateral pyramidal and cerebellar pathways and the gray matter on the right. *D* and *E*, section of the lower dorsal segments, showing destruction of the lateral pyramidal tracts; this gives the section a slight appearance of amyotrophic lateral sclerosis. Myelin sheath stain (Weil modification).

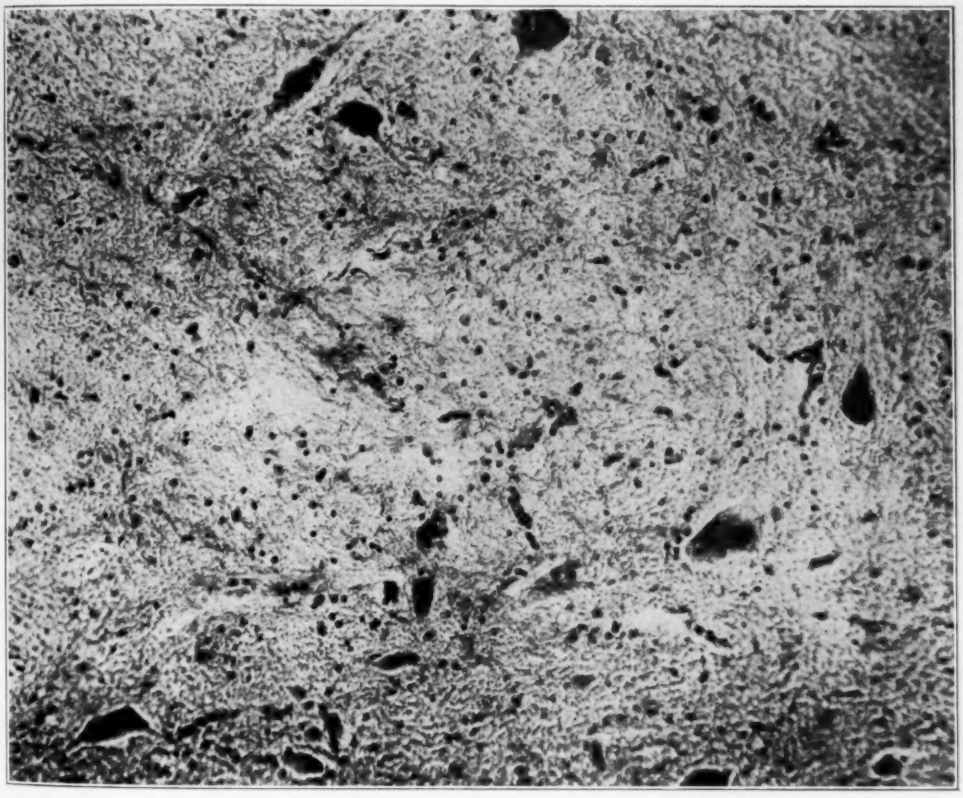

Fig. 7. (case 4).—Disappearance of the anterior horn cells in the left ventromesial group and replacement by glia fibers. The remaining nerve cells are shrunken and pyknotic.

Laboratory data, except for a gum mastic reaction of 5321000000, were negative.

Outcome.—The patient died at the age of 37.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis and carcinoma of the breast.

Autopsy.—Gross Examination: The white and gray matter of the cerebral hemispheres and the gray nuclear masses were riddled with plaques. The spinal

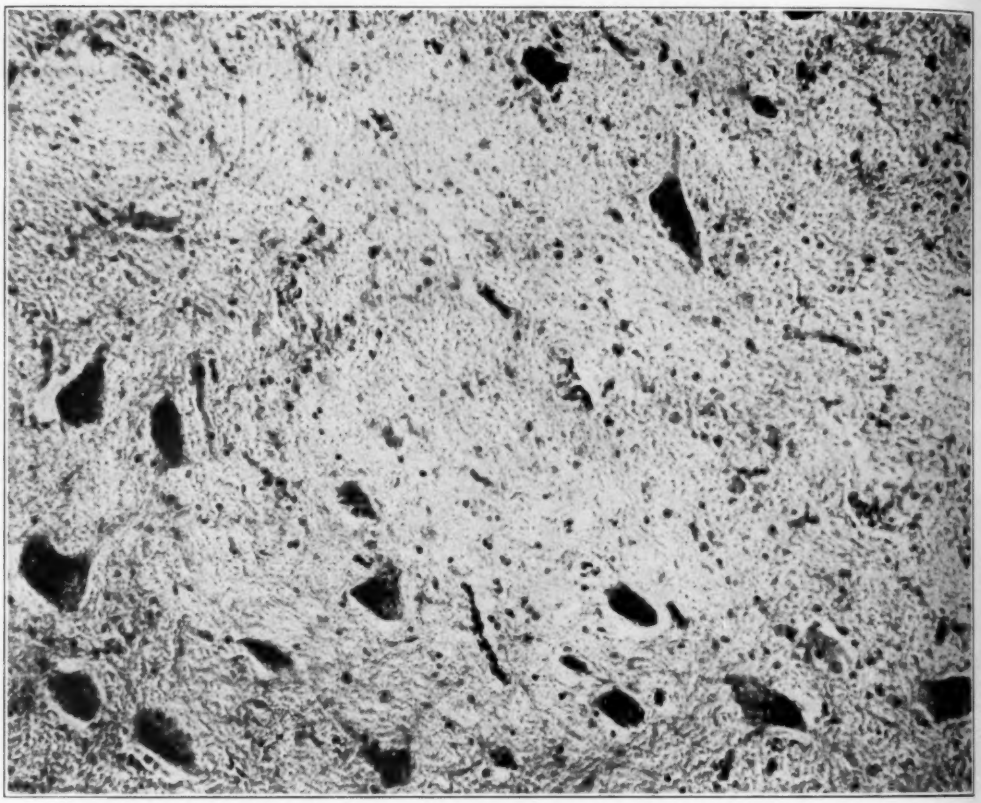

Fig. 8 (case 4).—Normal appearance on the right side. Cresyl violet stain; × 100.

cord appeared somewhat shrunken; numerous plaques were present throughout, mostly in the lower cervical and lower dorsal segments.

Microscopic Examination: In the spinal cord, plaques had destroyed most of the gray and white matter of the lower cervical segments (fig. 6, *A* and *B*). In the upper dorsal region a plaque had destroyed the columns of Goll and Burdach, the lateral pyramidal and the cerebellar pathways; the gray matter on the right was also involved (fig. 6 *C*). In the lower dorsal segments the plaques had destroyed essentially the lateral pyramidal tracts; the section with the myelin sheath stain resembled somewhat a picture of amyotrophic lateral sclerosis (fig. 6, *D* and *E*). In the cervical and dorsal segments most of the anterior horn cells of the left ventromesial group had disappeared and had been replaced by glia fibers and

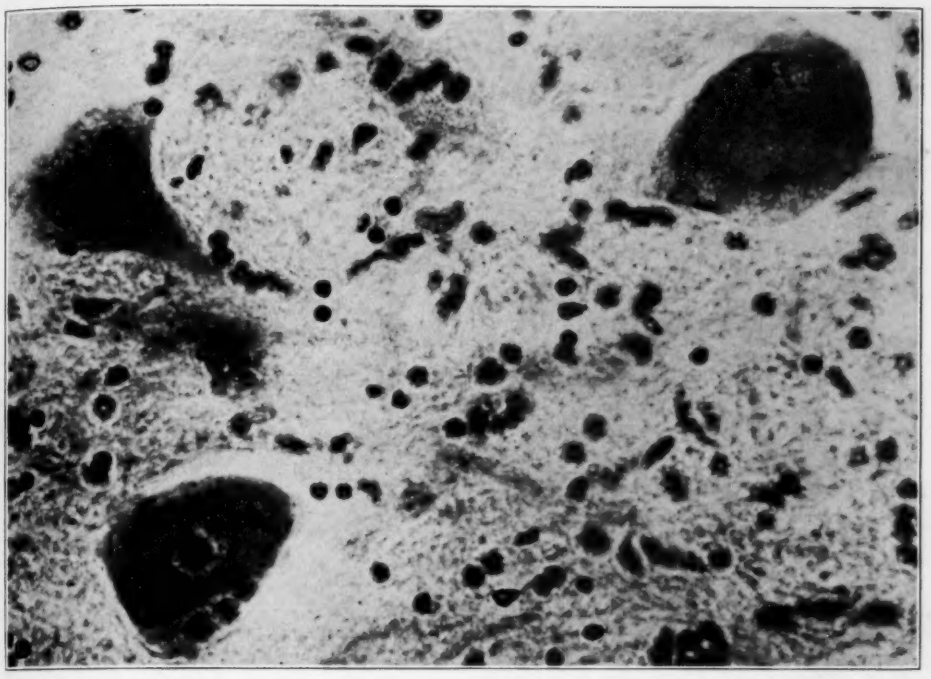

Fig. 9 (case 4).—Swelling and pigmentary atrophy of the anterior horn cells. Cresyl violet stain; × 480.

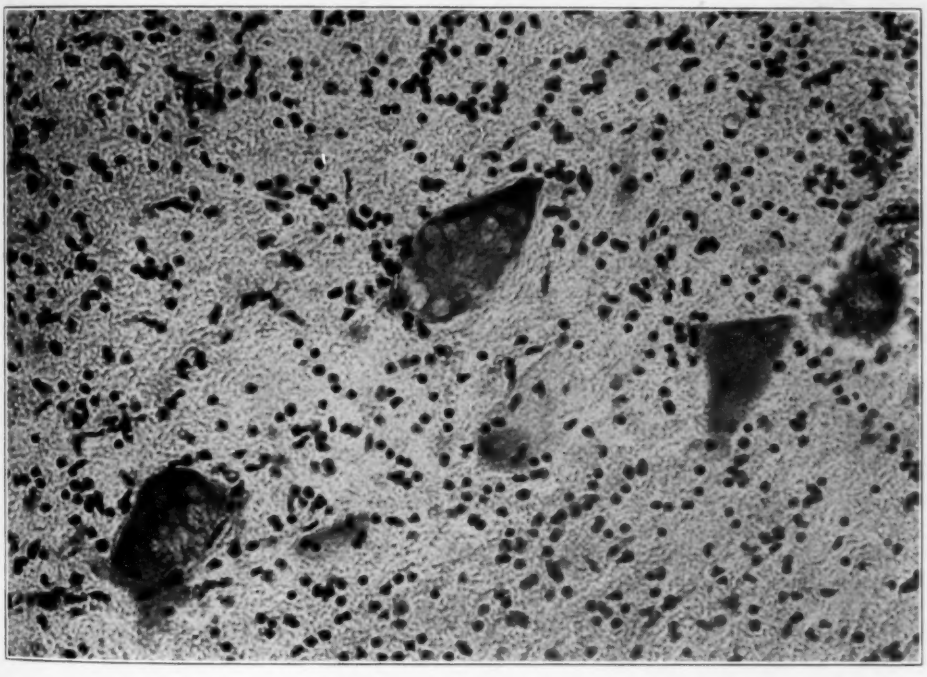

Fig. 10 (case 4).—Vacuolation of anterior horn cells. Cresyl violet stain; × 300.

cells (fig. 7). The remaining ganglion cells were shrunken and pyknotic. Swelling, pigmentary atrophy (fig. 9) and vacuolation (fig. 10) were also observed. In the lumbar region the outstanding changes in the anterior horn cells consisted of swelling, loss of chromatin and eccentric nuclei.

Comment.—As in the 3 previous cases, the clinical observation of atrophy of muscles was correlated with pathologic changes in the corresponding anterior horn cells.

CASE 5.—L. S., a man, aged 27, was admitted to the hospital with a history of an attack of sudden paresis of the right lower extremity at the age of 23, which

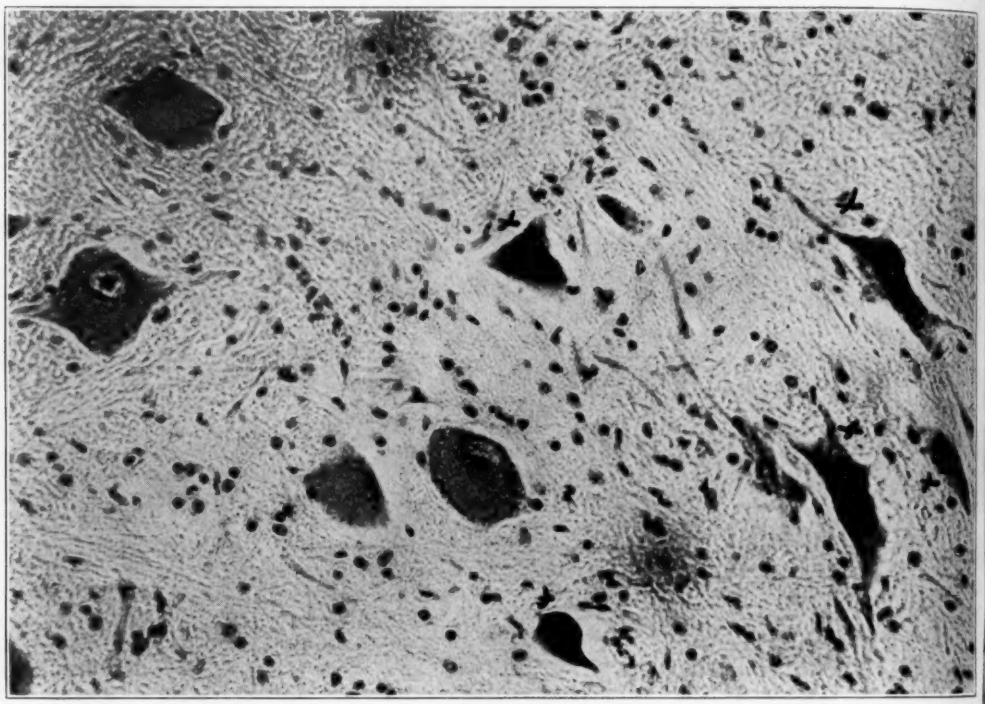

Fig. 11 (case 5).—Anterior horn cells from the left lumbar segment, showing swelling, pigmentary atrophy and sclerosis (x). Cresyl violet stain; × 240.

had lasted for eight weeks. He had been well until four years later, when both lower extremities became weak and incontinence of urine and feces developed.

Neurologic Examination.—This disclosed: marked nystagmus in all planes; atrophy of all muscles of the left lower extremity; complete flaccid paraplegia with areflexia; absence of the abdominal and cremasteric reflexes; bilateral ataxia; loss of all forms of sensibility from the eleventh dorsal segment down, except for the sense of position, which was impaired at and below the knees.

Laboratory data showed no abnormal condition except severe secondary anemia.

Outcome.—The patient died at the age of 28, following a severe urinary infection.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis.

Autopsy.—Gross Examination: The spinal cord was atrophic. On section, the gray matter of the lumbar region was translucent.

Microscopic Examination: A plaque of glia fibers had destroyed the entire white and gray matter of the lumbar region; the destruction was greater on the left than on the right. The anterior horn cells on the left showed various changes, the most outstanding being swelling, sclerosis (fig. 11) and pigmentary atrophy.

Comment.—The outstanding feature in this case was the atrophy of the left lower extremity with corresponding changes of the anterior horn cells of the lumbar region. The muscles of the hand, in contrast to the findings in the previous cases, had been spared.

CASE 6.—L. B., a man, aged 46, was admitted to the hospital with a history of tremor and transitory loss of power of the right lower extremity at the age of 20. Following this he had been well until seven years later, when weakness of the right lower and left upper extremities developed. Prior to admission there had been weakness of the left lower extremity and occasional incontinence of urine and feces.

Neurologic Examination.—There were: sluggish reaction of the pupils to light and no reaction in accommodation; weakness of the right side of the face; weakness of the left upper extremity and of both lower extremities; absence of the biceps jerks, hyperactive knee jerks, a bilateral Babinski sign and absence of the abdominal reflexes.

Laboratory data, except for a gum mastic reaction of 221111000, were negative.

Course.—At the age of 69 there were: bilateral internal strabismus; fibrillary tremor of the tongue, atrophy of the interossei, the thenar and hypothenar muscles and the muscles of the right leg and thigh; spastic paraplegia, and impairment of deep sensibility in both lower extremities and in the upper left extremity. The patient died suddenly at the age of 84.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis and carcinoma of the stomach.

Autopsy.—Gross Examination: In the brain, the vertebral arteries showed atheromatous changes; numerous fresh and old sclerotic plaques were scattered throughout the entire central nervous system.

The spinal cord (the thoracic and lumbosacral regions only were removed) was atrophic, and the fiber tracts could not be distinguished.

Microscopic Examination: In the spinal cord, sections of the midthoracic region revealed a plaque which had caused demyelinization of practically all the fiber tracts. Similar plaques destroying the white and gray matter were found in the lower dorsal region and in the lumbar and sacral regions. The anterior horn cells showed disintegration, vacuolation and chromatolysis.

Comment.—This case is of interest in that the patient lived for sixty-four years after the onset of the disease. Atrophy of muscles was noted fifteen years prior to death. We were unable to correlate the atrophy of the muscles of the hand with changes in the anterior horn cells of the corresponding cervical segments, as the entire cord was not secured at autopsy. The atrophy of the right lower extremity, however, was definitely caused by changes in the anterior horn cells in the lumbosacral segments.

CASE 7.—J. H., a man, aged 38, was admitted to the hospital with a history of impairment of vision in the right eye at the age of 32. This had been followed some time later by numbness and stiffness of both hands, tremor of the right upper extremity, unsteady gait, slow speech, frequency in urination and poor memory for recent events.

Neurologic Examination.—This revealed: the left pupil larger than the right and irregular and sluggish in its reaction to light; temporal pallor of the right disk; nystagmus; scanning speech; marked ataxia; intention tremor; marked atrophy of all muscles, "possibly due to disuse;" bilateral hyperreflexia and bilateral Babinski signs; diminished abdominal reflexes on the right and a diminished cremasteric reflex on the left, and diminished vibration and joint sense in all extremities. The patient was disoriented and intellectually deteriorated.

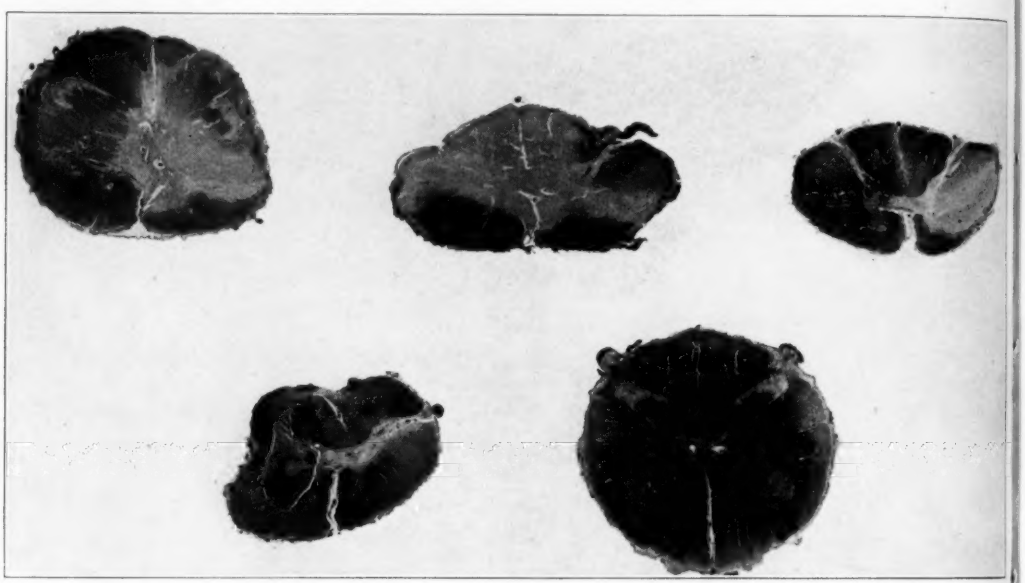

Fig. 12 (case 7).—Sclerotic plaques destroying the white and gray matter of the cervical, dorsal and lumbar segments. Myelin sheath stain (Weil modification).

Laboratory data were negative.

Outcome.—The patient died at the age of 56 of bronchopneumonia.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis, bronchopneumonia and hemangioma of the liver.

Autopsy.—Gross Examination: Fresh and old plaques were found in the white and gray matter of the cerebral hemispheres, thalamic nuclei and pons. No gross abnormalities were encountered in the spinal cord.

Microscopic Examination: In the spinal cord, sclerotic plaques involved the white and gray matter of the upper and lower cervical region and of the dorsal and lumbar regions (fig. 12). The plaques consisted of dense glial scars. The anterior horn cells of the segments mentioned disclosed homogeneization, sclerosis, pigmentary atrophy and vacuolation. Falling out of ganglion cells was also observed.

Comment.—The marked atrophy of all muscles, which was considered at the time of examination as being due possibly to disuse, is explained by the extensive destruction of the gray matter throughout the cord.

CASE 8.—L. S., a man, aged 60, was admitted to the hospital with a history of attacks of dizziness since the age of 40. Tremor of the head, diplopia, staggering gait, intention tremor and nocturia had developed later.

Neurologic Examination.—This revealed ticlike movements of the face. The right pupil was irregular and was larger than the left; both reacted sluggishly to light and in accommodation. There were also temporal pallor of the left optic disk; marked bilateral nystagmus; left corneal hypesthesia; tremor and ataxia of the upper extremities; scanning speech; atrophy of the small muscles of the hand; slight pyramidal tract signs, with bilateral Babinski sign; absence of the abdominal reflexes, and incontinence of urine.

Laboratory Data: The Wassermann reaction of the cerebrospinal fluid was reported as 3 plus on one occasion; there was an excess of globulin, with 16 cells. However, this was not confirmed on repeated examinations.

Course.—The patient had suffered from peptic ulcer for six years; otherwise the history in the hospital was uneventful until sudden death at the age of 60.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis.

Autopsy.—Gross Examination: Plaques had destroyed the white and gray masses of the cortex, mesencephalon and metencephalon. The spinal cord was slightly shrunken.

Microscopic Examination: The segments of the spinal cord were normal except for a small plaque in the white and gray matter of the cervical segments. The changes in the ganglion cells were similar to those described in the previous 7 cases.

Comment.—The atrophy of the small muscles of the hands, which was recorded fourteen years before death, was corroborated by the corresponding alterations in the anterior horn cells. There was no evidence of syphilitic lesions in the central nervous system.

CASE 9.—A. S., a woman, aged 35, was admitted to the hospital with a history of transitory weakness of the lower extremities and numbness of the upper extremities at the age of 16. At the age of 23 tremor of the left leg, left arm and head had developed.

Neurologic Examination.—This disclosed: irregular pupils; bilateral temporal pallor of the optic disks; nystagmus in all planes; generalized intention tremor; hemiparesis of the left hand; atrophy of the muscles of the shoulder girdle, the right upper extremity, the left biceps and the left lower extremity; bilateral pyramidal tract signs; absence of the abdominal reflexes; scanning speech, and slight emotional instability.

Laboratory data were negative except for the occasional occurrence of sugar and albumin in the urine.

Outcome.—The patient died at the age of 44 of bronchopneumonia.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis.

Autopsy.—Gross Examination: In the brain, sclerotic plaques were scattered throughout the white and gray matter of the thalamic and subthalamic nuclei. Plaques involved the gray and white matter throughout all the segments of the spinal cord.

Microscopic Examination: In the lower cervical segments of the spinal cord, a plaque had destroyed the gray as well as the white matter. Most of the anterior horn cells, especially in the ventromesial group, had been replaced by glia cells and fibers; the surrounding cells showed sclerotic changes. Plaques were also present in the midthoracic and lumbar segments. In the left side of the lumbar enlargement the anterior horn cells contained little Nissl substance and were shrunken; the nuclei were displaced to the periphery. The better preserved cells disclosed evidences of pigmentary atrophy.

Comment.—In this case the widespread muscular atrophy was correlated with lesions of the anterior horn cells in practically all the segments of the cord.

CASE 10.—L. F., a man, aged 37, was admitted to the hospital with a history of difficulty in walking since the age of 34.

Fig. 13 (case 10).—Sections of the cervical, dorsal and lumbar segments, showing destruction of the white and gray matter by multiple sclerotic plaques.

Neurologic Examination.—This disclosed: the right pupil slightly larger than the left; both pupils slightly irregular and reacting sluggishly to light; pallor of both optic disks; lateral and vertical nystagmus; marked intention tremor of the head and upper extremities; atrophy of the interosseal groups and the left thenar eminence; exaggerated deep reflexes; bilateral ankle clonus, with a positive Babinski sign; absence of the abdominal and cremasteric reflexes; slow, monotonous and scanning speech, and marked emotional instability.

Outcome.—Bronchopneumonia developed and the patient died at the age of 44.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis, hypernephroma of the left kidney and bronchopneumonia.

Autopsy.—Gross Examination: Plaques were present throughout the entire white and gray matter of the cerebral hemispheres. Areas of discoloration of the gray and white matter were observed throughout all the segments of the spinal cord.

Microscopic Examination: In the spinal cord, a large glial plaque had destroyed the gray and white matter of the left side of the seventh cervical segment. There was falling out of ganglion cells in the ventromesial, ventrolateral, intermediate and dorsolateral groups. The remaining cells were shrunken and pyknotic, and their axons had spiral-like prolongations. Pigmentary atrophy was also observed. The white and gray matter of most of the cervical, dorsal and lumbar segments had been destroyed by plaques (fig. 13). The ganglion cells showed the same pathologic changes as at the seventh cervical segment. In the lumbosacral region two plaques had destroyed the lateral pyramidal tracts, and the cord had the appearance of a section in amyotrophic lateral sclerosis (fig. 14).

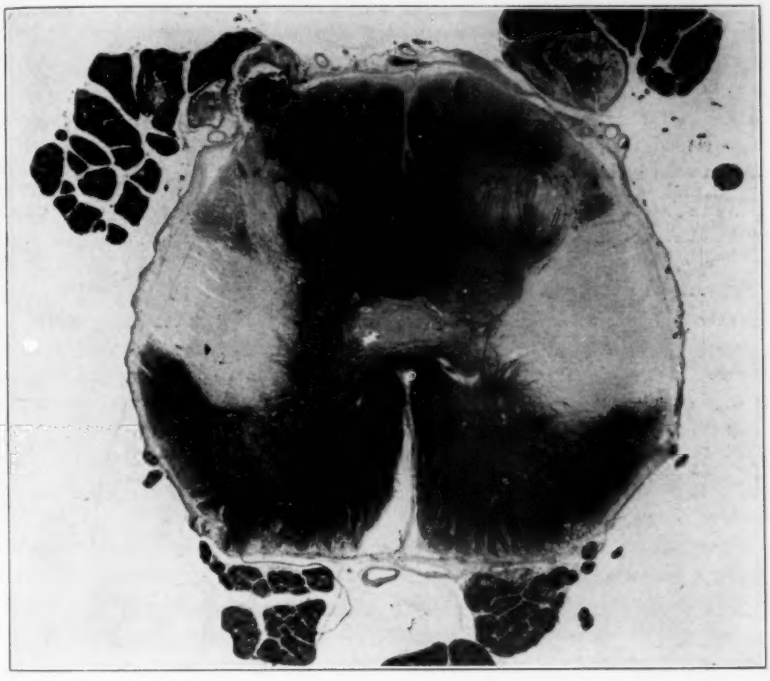

Fig. 14 (case 10).—Section from the first sacral segment, in which two plaques have destroyed the lateral pyramidal tract, giving the cord the appearance of a section seen in amyotrophic lateral sclerosis. Notice also the partial destruction of the gray matter. Myelin sheath stain (Weil modification).

Comment.—The atrophy of the interossei and the left thenar muscles was due to the plaque which involved the gray matter of the lower cervical segments. Of interest is the bilateral demyelinization of the crossed pyramidal tract in the lumbosacral region, resembling pathologically a picture of amyotrophic lateral sclerosis.

Case 11.—P. S., a man, aged 46, was admitted to the hospital with a history of impotence since the age of 30 and of difficulty in walking, weakness and slight urinary incontinence since the age of 38.

Neurologic Examination.—This disclosed: nystagmus, a tendency to fall to the left, tremors of the head and body, a marked Romberg sign, ataxia of the upper extremities, adiadokokinesis, atrophy of the right sternocleidomastoid and interossei muscles and of the thenar hypothenar eminences, bilateral pyramidal tract signs and absence of the abdominal reflexes

Outcome.—The patient died at the age of 49 from an unknown cause.

Laboratory data were negative.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis.

Autopsy.—Gross Examination: Plaques had involved the white and gray matter of the cerebral convolutions and other nuclear masses. In the spinal cord, a plaque had destroyed the right posterolateral columns and the gray matter of the lower cervical region.

Microscopic Examination: The lower cervical region showed involvement of the gray matter and most of the white matter on the right side of the cord. The changes in the anterior horn cells of the ventrolateral and ventromesial groups conformed with those described in the previous 10 cases. Most of the destroyed ganglion cells had been replaced by glia cells and fibers.

Case 12.—E. D., a man, aged 38, fell out of a car at the age of 33; seven months later he could not lift his feet properly. At the age of 38 his right foot was run over by a truck. Weakness, tremor of the legs and sphincteric disturbances then developed.

Neurologic Examination.—This revealed: spastic gait, nystagmus, paresis of the upper extremities, bilateral pyramidal tract signs and atrophy of the interossei muscles. Memory was poor, and at times the patient was disoriented. At the age of 45 he had begun to have generalized convulsions, which had recurred at infrequent intervals until death at the age of 48.

Diagnosis.—The clinical and anatomic diagnosis was multiple sclerosis.

Autopsy.—Gross Examination: There was translucency of the fiber tracts in the cervical region of the spinal cord.

Microscopic Examination: A sclerotic plaque had destroyed most of the fiber tracts and gray matter of the lower cervical segments. The anterior horn cells had undergone severe pathologic changes similar to those in the previous 11 cases.

Comment.—This patient had had sphincteric disturbances for ten years and atrophies five years prior to death.

GENERAL COMMENT

An analysis of the 12 cases reported disclosed that the small muscles of the hand were most frequently involved; in only 1 instance (case 5) was there no atrophy of these muscles. In case 2 the other groups of muscles of the right upper extremity and of the tongue were also atrophied. In case 4 there was, in addition, atrophy of the muscles of the lower extremities. In case 5 the muscles of the lower extremities only were involved. Cases 1 and 7 also showed atrophy of all groups of muscles. In case 9 there was atrophy of the muscles of the shoulder girdle, the right upper and left lower extremities and the left biceps. In case 11, in addition to involvement of the muscles of the hand, the right sternocleidomastoid was atrophied.

Of 110 patients observed clinically, most of whom are still living, 17 showed atrophies of muscles. Of these, 11 showed atrophy of the muscles of the hand; 4 of the pectoral muscles; 2 of the gluteals; 1 of the deltoid; 1 of the sternocleidomastoid; 2 of the masseter, and 3 of the muscles of the tongue.

Analysis of the time when the atrophies appeared in the group which came to necropsy shows that in most patients the atrophies preceded death by from one to fifteen years. The atrophies were noted fifteen years prior to death in case 6, fourteen years before death in case 8 and five years before death in case 12. In all other cases the atrophies were observed when the patients were first seen at the hospital, and it is impossible to state how long they had existed prior to death.

In addition to atrophy of the muscles, some patients presented mental changes and sphincteric disturbances. Marked emotional instability, defect of memory, disorientation, poor insight, paranoid trends and confusion were found in cases 3, 7, 10 and 12 of the clinicopathologic group. Similar observations were recorded in only 2 cases of the clinical group. Urinary and fecal incontinence were found in the clinicopathologic cases 1, 5, 6 and 12; urinary disturbances alone were found in cases 3, 4, 7, 8 and 11. In the clinical group, urinary sphincteric disturbances were present in 13 cases, and fecal disturbances in only 1.

The anterior horn cells corresponding to the muscles involved showed pathologic changes. In most of the nerve cells the alterations were due to the invasion of the gray matter by the plaques. The outstanding pathologic changes of the cells consisted of shrinkage and pyknosis (sclerosis), chromatolysis, swelling, vacuolation and complete disappearance of the ganglion cells. So-called axonal degeneration was also observed. The most common finding was sclerosis of nerve cells, a pathologic process usually observed in chronic diseases of the nervous system. The sclerosis of the nerve cells is not surprising when one considers the chronicity of multiple sclerosis. The gray matter invaded by the plaque showed in most cases replacement by glia fibers and cells. On the basis of these findings we can state that most of the changes in the ganglion cells were primary and were not due entirely to axonal degeneration. In cases 4 and 10 there was also bilateral demyelinization of the crossed pyramidal pathways, and the sections gave a picture resembling that of amyotrophic lateral sclerosis.

The most intensive study of atrophies in multiple sclerosis was made by Lejonne [1] in 1903. He studied 10 cases, 3 of which came to necropsy. The muscles most frequently involved in Lejonne's group were those

1. Lejonne, M. P.: Contribution à l'étude des atrophies musculaires dans la sclérose en plaques, Thèse de Paris, G. Steinheil, 1903.

of the lower extremities. In his cases the interossei were more frequently affected than the muscles of the thenar and hypothenar eminences; in the forearm the extensors of the fingers were involved more often than the flexors; in the arms, the biceps and anterior brachials were most commonly affected, and in the lower extremity the extensors were affected more frequently than the flexors. We cannot subscribe to such a strict classification of atrophy, for in our group the plaque which invaded the gray matter did not limit itself to a special group of cells. In our cases the muscles of the hand were most frequently affected; this is readily explained when reference is made to the sections in which it can be seen that the gray matter of the lower cervical part of the cord was the region most frequently invaded by the plaques.

Lejonne also stated that multiple sclerosis associated with atrophy of muscles is characterized by the precocity of the sphincteric disturbances, trophic disorders and mental changes. As has already been pointed out, 4 of our patients showed mental symptoms, and disturbances of one or both sphincters were observed in 8 of the 12 cases. The trophic disturbances are possibly the end-result of confinement to bed. Our patients showed no trophic disturbances, and we are inclined to attribute this to the care which these bedridden patients received. Lejonne [1] also found a typical amyotrophic picture in many of his patients. In our cases 4 and 10 there was destruction of both crossed pyramidal tracts, and it is only on histopathologic grounds that one might have made the error of diagnosing the condition as amyotrophic lateral sclerosis. Clinically, none of our patients showed the syndrome of Charcot's disease in its pure form. The onset, progress and neurologic signs and symptoms in all the cases were such that not once was the error made of calling the condition amyotrophic lateral sclerosis.

Cases of disseminated sclerosis which simulated amyotrophic lateral sclerosis were described by Charcot,[2] Pitres,[3] Dejerine,[4] Bouchaud [5] and Thomas and Comte.[6] Marked muscular atrophy in this disease was

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2. Charcot, J. M.: Leçons sur les maladies du système nerveux, Paris, 1877.

3. Pitres, A.: Contribution à l'étude des anomalies de la sclérose en plaques disseminée, Rev. de méd. **1**:893, 1877.

4. Dejerine, J.: Etudes sur la sclérose en plaques cérébrospinale à forme de sclérose latérale amyotrophique, Rev. de méd. **4**:193, 1884.

5. Bouchaud: Sclérose en plaques avec amyotrophies, J. de neurol. **5**:348, 1900.

6. Thomas, A., and in Comte, cited in Dejerine, J., and Thomas, A.: Maladies de la moelle épinière, Paris, J. B. Baillière et fils, 1909, p. 1404.

also described by Brauer,[7] Probst,[8] Wegelin,[9] Schnitzler,[10] Spiller [11] and others. Most of these authors described changes in the anterior horn cells somewhat similar to those recorded by us.

CONCLUSION

1. In 12 cases of multiple sclerosis of a group of 20 which came to autopsy and in 17 of a group of 110 which were observed clinically, atrophy of muscles was found.

2. The muscles of the hand were atrophied in most cases; those of the upper and lower extremities were less frequently affected, and the muscles of the shoulder girdle and of the face were least frequently involved.

3. Four of these atypical cases of multiple sclerosis were associated with mental changes.

4. Histopathologically, the atrophy of muscles was due to destruction of the anterior horn cells. The changes in the nerve cells consisted of sclerosis, chromatolysis, vacuolation, pigmentary atrophy, retrograde degeneration and complete disappearance of cells. The gray matter was replaced by glia fibers and cells. The most frequent site of the plaques in the gray matter was in the lower cervical region.

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7. Brauer, L.: Muskelatrophie bei multipler Sklerose, Neurol. Centralbl. **17**:635, 1898.

8. Probst: Zur Kenntnis der disseminierten Hirn-Rückenmarksklerose, Arch. f. Psychiat. **24**:570, 1901.

9. Wegelin, F.: Ueber akut verlaufende multiple Sklerose, Deutsche Ztschr. f. Nervenh. **31**:354, 1906.

10. Schnitzler, J. G.: Klinische Beiträge zur Kenntnis der Muskelatrophien laufenden formen von multipler Sklerose und chronische Myelitis, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**:310, 1912.

11. Spiller, W. G.: A Report of Two Cases of Multiple Sclerosis with Necropsy, Am. J. M. Sc. **125**:167, 1903.

PELLAGRA IN ASSOCIATION WITH CHRONIC ALCOHOLISM

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The rôle which alcohol plays in the production of lesions in the nervous system is still obscure. Even in the early editions of his textbook of psychiatry, Kraepelin stated that many such lesions could not be explained on the basis of the toxic effects of alcohol alone and that some other factor, such as a disturbance of metabolism of unknown etiology, must be involved. As early as the year 1869, Leudet [1] recognized that pellagra, a disease usually characterized by changes in the nervous system, dermatitis and diarrhea, was frequently complicated by chronic alcoholism. He distinguished, however, the pellagra complicated by alcoholism, which he called pseudopellagra, from the genuine or uncomplicated form. Since the time of Leudet, opinion has been radically divided on the question of the relationship of these two conditions. Tuczek,[2] Babes and Sion [3] and Kozowsky [4] maintained that alcohol, in common with poor nutrition, neglect and poverty, frequently served as a predisposing factor in pellagra. The frequency of association of these two conditions has also been stressed by Knowles and Ludy [5] and by Hall in a discussion of the paper on pellagra presented by Pierce.[6] On

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1. Leudet, E.: Recherches pour servir à l'histoire de la pellagre sporadique et de la pseudo-pellagre des alcoolisés. Memoire lu à la Société de biologie, Compt. rend. Soc. de biol. **4**:3, 1869.

2. Tuczek, F.: Ueber die Veränderungen im Centralnervensystem, speziell in den Hintersträngen des Rückenmarks, bei Ergotismus, Arch. f. Psychiat. **13**:99, 1882.

3. Babes, V., and Sion, V.: Die Pellagra, in Nothnagel, H.: Specielle Pathologie und Therapie, Vienna, Hölder, Pichler and Tempsky, A.-G., 1901, vol. 24.

4. Kozowsky, A. D.: Die Pellagra: Pathologisch-anatomische Untersuchung, Arch. f. Psychiat. **49**:204, 556, 873, 1912.

5. Knowles, F. C., and Ludy, J. B.: Pellagra as Observed at the Pennsylvania and the Philadelphia General Hospital, M. Clin. North America **10**:431, 1926.

6. Pierce, L. B.: Pellagra, Report of a Case, Am. J. Psychiat. **4**:237, 1924-1925.

the contrary, Rezza [7] and, indeed, many others hold that pellagra complicated by alcoholism is a different entity entirely from the uncomplicated cases. There is no one apparently who is of the opinion that alcohol has a direct or primary etiologic relationship to pellagra.

The question of the identity of the form of pellagra uncomplicated by chronic alcoholism with that form which is complicated by it will be answered only when the true etiology, exclusive of any contributing or secondary factor, is established. This can perhaps be studied best experimentally, and much has already been done toward a solution of the problem by this method. The discovery that pigeons and other animals developed polyneuritis on diets deficient in vitamin B indicates that the lack of vitamins may be important in the production of lesions in the nervous system of man as well. The comprehensive studies of Goldberger and his associates [8] proved that pellagra could be relieved by a diet rich in vitamins, especially in the vitamin B complex. Subsequently, Goldberger and his co-workers [9] were also able to produce experimentally in dogs by a diet which was deficient, among other factors, in vitamin B_2 a syndrome which in some ways resembled pellagra. On the basis of poverty and neglect, with the accompanying malnutrition, it was easy to account for instances of pellagra, but it seemed difficult to conceive that deficiency diseases could occur in people who were living on the ordinary varied diet of the more fortunate Americans and Europeans. In such people, however, the excessive use of alcohol may be associated with neglect of food and loss of appetite, or even with poor assimilation of the food ingested, and may ultimately produce a picture of dietary deficiency. It is a curious fact that such a deficiency disease as pellagra tends to appear in people who drink distilled liquors and but rarely in those who drink wine or beer.

The problem of the identity of pellagra with the deficiency disease complicated by chronic alcoholism may also be studied anatomically in man. A comparison of the findings in these two conditions should throw some light on this question. The following cases are presented for this purpose and also because they serve as examples of the principle that pictures of deficiency disease may arise in association with chronic alcoholism by the mechanism just outlined. Emphasis will be laid on the fact that a knowledge of the mechanism of this disease may be utilized therapeutically with satisfactory results.

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7. Rezza, A.: Beitrag zur pathologischen Anatomie der Pellagrapsychosen, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**:1, 1912.

8. Goldberger, J.; Waring, C. H., and Tanner, W. F.: Pellagra Prevention by Diet Among Institutional Inmates, Pub. Health Rep. **38**:2361, 1923.

9. Goldberger, J.; Wheeler, G. A.; Lillie, R. D., and Rogers, L. M.: Further Study of Experimental Blacktongue with Special Reference to Blacktongue Preventive in Yeast, Pub. Health Rep. **43**:657, 1928.

REPORT OF CASES

CASE 1.—*History.*—F. Y., a Lithuanian, aged 48, married, was admitted to the Medical Service of the New Haven Hospital on April 11, 1931. His legs were too weak for him to walk, and he appeared disoriented as to time and place, but not as to person. No information as to heredity was obtained. The wife and five children were living and well. The patient came to this country about twenty-two years before examination and had always worked as a laborer. Until five years before he had always been well and was said to have been of unusually strong physique. In his last job he carried large molten hot bars of brass, but had not found this work hard. Five years previously to his entrance into the hospital he had been in bed with "pneumonia," and after this began drinking a great deal. He became "nervous" and irritable, and he frequently had no appetite.

Although up to this time the patient had been a steady drinker, he had never drunk enough to interfere with his work. Sixteen months before admission to the hospital there developed generalized weakness, tremor accompanied by headache, loss of appetite, nausea, vomiting and dizziness. These symptoms lasted about a week, but he did not entirely recover from them and was forced to change to lighter work. Exacerbations of the same symptoms recurred several times, and he came to the outpatient clinic four months before admission to the hospital. In addition to these symptoms he then had pain in the abdomen and painful micturition of more recent onset.

When seen at the clinic the patient was a heavy-set, well developed man, weighing 165 pounds (74.84 Kg.), with large erythematous patches on the skin of the face. The gums were red and swollen, but the tongue was not described as abnormal. The prostate was slightly enlarged; a prostatic smear revealed no evidence of gonorrhea. There were a few varicose veins on the legs and patches of an apparent dermatitis over the ankles. Neurologic examination gave negative results. The diagnosis at that time was chronic alcoholism.

After the first visit to the outpatient clinic, the patient worked for a few days, drank a "good deal" and had a recurrence of symptoms with increased severity. He became too weak to leave bed and complained of pains "all over." He had very little appetite, eating little more than bread and potatoes. Two weeks before admission he began to "wander in his speech," to laugh in a silly fashion, and to say that he saw babies walking with men on the wall. His relatives were unable to remember many other queer statements that he made.

Examination.—On admission to the hospital the patient was uncooperative, mumbled to himself and often tried to get out of bed, but was usually too weak even to sit up. It was always impossible for him to stand. The tongue was red and slightly swollen. The gums were inflamed, swollen and soft, and there were many carious teeth. Some scaling of the skin was present over the hands and feet, but there was no definite increase in pigmentation. The pupils reacted sluggishly but equally to light and in accommodation. There were marked weakness and slight atrophy as well as some spasticity of the left arm and of both legs. Spasticity was most marked in the left leg. Deep and superficial reflexes were present, but were much more active on the left side than on the right. There was a sustained bilateral ankle clonus. The plantar responses were flexor in character. There appeared to be hyperesthesia to superficial and deep pressure over the left arm and leg. The vibratory sense could not be tested.

The laboratory findings were: Blood: red cells, 4,800,000; hemoglobin, 90 per cent; white cells, 8,000, with a normal differential count; slight anisocytosis; no stippled cells. Kahn test negative. Cerebrospinal fluid: pressure, 110 mm.; clear

and colorless; 4 cells; negative Pandy and Ross-Jones tests; negative Wassermann reaction. Urine: specific gravity, from 1.022 to 1.030; otherwise normal.

The patient was conspicuously disoriented as to time and place; he was restless, and his mood was very labile. He mumbled to himself in an unintelligible fashion and seemed to be expressing himself in a mixture of languages. His family could understand only occasional phrases.

Course.—These symptoms and signs became more pronounced. The temperature ranged between 98 and 100 F.; the pulse rate was between 70 and 100 per minute; the respiratory rate remained about 20. The blood pressure was 120 systolic and 90 diastolic.

The patient was difficult to nurse and to feed, and as a result only small amounts of a diet rich in vitamins, yeast cake and vitavose [10] were ingested at irregular intervals. There was no diarrhea at any time. The condition grew progressively worse, and the patient died with a terminal pneumonia two weeks after admission to the hospital.

Necropsy.—The examination was begun one hour and forty minutes post mortem by Dr. M. T. Shelton. The important observations were: The body was well developed but somewhat undernourished, measuring 168 cm. (66 inches) in length and weighing 51 Kg. (112 pounds). The dorsum of the tongue and the buccal mucous membranes were red and had a granular appearance. Many of the teeth were missing, while others were carious. The gums at the roots of the teeth were covered with a yellow exudate. A superficial decubitus, measuring 6 cm. in diameter, was present over the sacrum; the skin over the rest of the body was not abnormal in any way. The left arm was slightly smaller than the right, and its muscles were flabby. Focal pneumonia was found grossly in the lower lobe of the right lung, and this was confirmed by microscopic examination. Careful examination of the whole gastro-intestinal tract revealed no lesions.

There was no exudate in any part of the subarachnoid space. The pial vessels over the convexities of the cerebrum were intensely congested. Frontal section of the cerebral hemispheres revealed well defined cortical gray matter of the usual width. The centrum ovale and the basal ganglia were not abnormal. The ventricles were not dilated, and the ependyma was smooth and glistening. Examination of the substantia nigra revealed nothing unusual; this was also true of the cerebellum, medulla and spinal cord.

Blocks of the brain and spinal cord were removed and prepared for histologic examination by the Nissl method, the sudan III method for fat, the Bielschowsky method for axons, the Spielmeyer method for medullary sheaths and the Holzer method for neuroglia. Unfortunately, the peripheral nerves were not removed for examination, and no Marchi preparations were made. Subsequently, when the desirability of preparations stained by this method was apparent only formaldehydized tissue was available, which precluded the utilization of this staining technic.

Microscopically, no exudate of any kind was found in the cerebral and spinal leptomeninges. The cortical cyto-architecture of the cerebrum was normal, but the individual nerve cells of the cortex showed distinct changes in the Nissl preparations. These changes were most marked in the frontal lobes, particularly in the precentral convolutions. They consisted of rounding and swelling of the cell bodies in which the cytoplasm had a turbid appearance and was indistinct; the tigroid substance in most of the cells was absent, and the nuclei appeared small and eccentrically placed. In the giant cells of Betz and in the motor cells of the

10. Vitavose is a soluble vitamin B preparation made from wheat germ.

anterior horns of the spinal cord the cytoplasm had a hyalin-like appearance, and the nuclear eccentration was marked (fig. 1). The appearance of these cells was identical with that seen in the "axonal" type of reaction. Many of the cortical nerve cells contained large quantities of lipoid material which stained brilliant red by the sudan III method. There was no glial proliferation in the cerebral gray and white matter. The only exception to this was a large glia rosette in the white matter below the sixth cortical lamina.

The cerebral blood vessels were, on the whole, normal. Occasional cortical arterioles, however, were unduly prominent by virtue of the fact that their walls showed cellular proliferation, were thickened and had a hyaline appearance.

There was no reaction of any kind in the periventricular gray matter, the floor of the fourth ventricle or the mamillary bodies. These regions were also free from small hemorrhages. The absence of any lesions in these parts of the brain excluded an "alcoholic" encephalitis of the Wernicke type.

The most striking changes by far were those in the spinal cord. In addition to the "axonal" changes already described in the cells of the anterior horns, the stains for medullary sheaths revealed a picture of degeneration which was scattered partly in the pyramidal and partly in the sensory tracts. The foci of degeneration were small and could be demonstrated in the sudan III preparations as well as in those stained by the Spielmeyer method. Bielschowsky preparations demonstrated a loss of the intraganglionic fibrillae of the cells that were seen to be changed in preparations stained by other technics, but the axons in both the cerebrum and the spinal cord appeared to be unaltered. Holzer preparations of the spinal cord showed a slight but definite increase in neuroglia fibers which was most marked in the crossed pyramidal tracts.

Comment.—This patient had no cutaneous lesions and no diarrhea. A red, swollen tongue and neurologic and mental changes in a patient who was malnourished as the result of marked loss of appetite suggested the diagnosis of pellagra. That such a diagnosis was warranted was revealed by the anatomic study of the nervous system. This will be commented on more fully later in the discussion of all three cases.

As regards the treatment of this patient it must be stated that he was given merely the ordinary hospital diet by spoon feeding and an adequate amount of fluids. He presented a difficult nursing problem, and it proved impossible to feed him substances rich in vitamins with any regularity. Removal of alcohol from the diet brought about no remission of symptoms.

CASE 2.—*History.*—A. Z., a white, married woman, aged 24 years, was admitted to the Psychiatric Clinic on March 26, 1932. Her legs were in a position of semiflexion, and she showed a state of mental confusion, with considerabe agitation, fright and apprehensiveness. Both her parents were Lithuanians. The father was a farmer, aged 55, and a chronic drinker. The mother, aged 50, apparently had a very low grade of intelligence and was also alcoholic. Nothing was known of the grandparents. The patient had three siblings, aged 20, 18 and 16, respectively; none of them had abnormalities as far as was known. The patient's husband, aged 25, stated that he had a penile sore three years after marriage, but serologic tests had been continually negative; no treatment had been given. The patient had been married for six years, and had had two early miscarriages

with no other pregnancies. Home conditions were fairly satisfactory, although the husband earned very little.

The patient's husband asserted that for many months previous to the onset of the present illness the patient was regularly accustomed to take two or three "small gin snifters" before each meal. She had apparently consumed as much as from a pint to a quart of alcohol daily, which she bought from a nearby speakeasy; not infrequently, on returning home at night, the husband found her moderately intoxicated. She also received considerable quantities of home brew from her father. The patient drank very heavily until Jan. 1, 1932; since then she was said to have stopped drinking "hard liquor," but continued to drink "moderate" quantities of wine. There is little doubt that she consumed a considerable amount of a very inferior grade of alcohol over a long period of time. During the last six months she ate little more than bread and coffee.

The first symptoms of the patient's present condition occurred in May, 1931, when she and her husband were returning home from a meeting. When about 50 feet from the house the patient suddenly said to her husband, "Hold me, my feet are giving in." When he led her into the house the husband noticed that the patient's legs were stiff and that her head was hyperextended, apparently in an opisthotonic manner. There were no convulsions. She was confused, but when put to bed lay quietly. This attack lasted about ten or fifteen minutes, when the patient again became oriented; but she had a complete amnesia for this period. She slept well that night and on the next day was able to be up and about, but could walk only in a stiff-legged manner. As time went on the condition of the legs became worse. They were weak and it became necessary for her to grasp nearby objects for support in walking.

The patient's physical condition also became progressively worse, but she remained completely oriented and apparently rational. On Jan. 1, 1932, after a New Year's Eve party, she suddenly became confused and "talked queer things." A doctor who was called at this time said that she had a "touch of paralysis," which was interpreted by the husband to mean poliomyelitis. She was hospitalized in her home town for eight days, during which she had frequent convulsions and was often delirious. Occasional incontinence was also present, but disappeared after discharge from the hospital. The confused state, however, persisted to the time of her admittance to the Psychiatric Clinic in March, 1932.

Examination.—On admission the patient was agitated and expressed many delusions. She muttered unintelligibly and had hallucinations. She frequently cried bitterly as if in the presence of something which frightened her terribly. She did not describe or name any hallucinations, except on one occasion when she mentioned that animals were about her. Generally she was apathetic and smiled only rarely.

Her weight on admission was 90 pounds (40.82 Kg.); she was emaciated, and the musculature of the arms and legs showed atrophic changes. The legs were held constantly in a position of semiflexion and were very spastic. She complained of pains in the legs, particularly in the soles of the feet. Examination of the cranial nerves gave negative results, except for a fine tremor of the lower part of the face and fine and coarse tremors of the tongue. All the deep reflexes were extremely hyperactive, and there was a well sustained bilateral ankle clonus. The abdominal reflexes were absent. There were no other pathologic reflexes, except a bilateral positive Hoffmann's sign. The patient had vesical incontinence. She could stand, but there was little strength in the arms and legs. There was considerable fibrillary twitching of the musculature of the face, arms and hands.

Coordination was profoundly disturbed in the arms, but could not be tested in the legs because of the spasticity. There was an inconstant dysarthria. Pain was not produced by pressure along the peripheral nerve trunks. There was a questionable damage in proprioceptive sense perception in both legs, but no other sensory disturbances were noted.

Examination of the urine gave negative results except for a slight trace of albumin. The red blood cells were normal in number, but slight poikilocytosis was present. The Kahn test of the blood was negative. Examination of the spinal fluid revealed an initial pressure of 75 mm., with no changes in the Queckenstedt test; there were no cells in the fluid; the Pandy test was 2 plus; the Ross-Jones, the Wassermann and the colloidal gold tests all gave negative results.

Course.—On admission the patient was given a diet adequate in vitamins A and B, and in addition received 2 tablespoonfuls of vitavose daily and egg-nogs. The legs were put in Osgood splints, and physical therapy was utilized daily. Disorientation soon disappeared, as did the vague ideas of delusion and the hallucinations. Memory for recent events remained poor, however, until shortly before discharge, when it was completely recovered. She complained less and less about the pain in the legs. Incontinence ceased and coordination of movements in the arms was restored; twitchings in the arms and legs were much diminished. With the exception of considerable whining and complaining when her relatives were about, the patient seemed cheerful. The left leg became completely relaxed, mobile and free from pain; recovery of the right leg was considerable, although some flexion deformity and pain persisted. The weight rose from 90 pounds on admission to 103 pounds (46.71 Kg.) at the time of discharge from the hospital on June 7, 1932.

Comment.—This patient, like the first, had no cutaneous lesions and no diarrhea; moreover, the tongue was normal. The signs and symptoms of disease in the nervous system, however, were much alike in both, except that this patient showed much more spasticity of the legs and also contractures.

The dietary treatment of these two patients differed considerably. Whereas the first received only the usual hospital diet, the second was given a special diet rich in vitamins. A slow but steady improvement occurred. The appetite, poor at first, steadily improved and, at the time of discharge from the hospital, was excellent. Symptoms of disease in the nervous system improved much more slowly than did the weight and appetite. When seen eight months after discharge from the hospital, the patient appeared to have made an almost complete recovery. Her weight was 140 pounds (53.50 Kg.), she was able to walk with the aid of a cane and could do housework. There was no evidence of impairment of mental functions. Weakness of the left leg seemed to be the only residual evidence of the illness. She reported that her appetite was excellent, that she was eating from four to eight eggs a day, a variety of vegetables and some meat, such as chicken or corned beef. It is noteworthy that she admitted that she was still drinking "a little" cider and home brew. Based on this remarkable

outcome it seems reasonable to suggest that if the first patient had been given large quantities of vitamins, particularly the vitamin B complex, he too might have responded favorably.

CASE 3.—*History.*—E. Z., a white, married woman, aged 39, was admitted to the medical service of the New Haven Hospital on June 27, 1932, and then transferred to the Psychiatric Clinic. She had been a chronic alcoholic for at least nine years and during the past year had been drinking as much as 3 or 4 pints of alcohol each week. In March, 1932, she experienced difficulty in walking and had pains in the legs; these were present at first only in the knees and calves; they were sharp, knifelike and intermittent. Numbness and alternating sensations of heat and cold followed the attacks of pain, and the patient took to bed. At this time she began to drink more heavily, frequently as much as from 1½ to 2 pints of whisky or gin each day. She soon lost appetite completely, ate very little, and began to lose weight rapidly. The pain in the feet increased in severity, and she was admitted to a hospital where the condition was diagnosed as alcoholic neuritis. She went home against advice, and the condition became worse. A change in personality, characterized by spells of crying and childish behavior, occurred shortly before her entrance into the New Haven Hospital. For several weeks preceding this the patient felt that she was losing her mind.

The past history revealed that she had acquired syphilis at 18 years of age and received two intravenous injections, refusing further treatment. Symptoms or signs indicative of secondary or tertiary lesions, however, had never been noted. At the age of 27 she married a man twenty-three years her senior, whom she soon left because of his alcoholism. She herself did not drink at this time. Four years later she married her present husband, who began drinking at about that time and became a chronic alcoholic. The two often drank together, and the patient also frequently drank alone. In November, 1931, she had an appendectomy and a salpingectomy for a "pus tube."

The family history is similarly replete with instances of chronic alcoholism. The patient's father is said to have drunk alcohol but not to excess. An older sister has a son who was formerly a patient in the Psychiatric Clinic with an alcoholic psychosis. Another sister of the patient is a chronic alcoholic.

Examination.—On admission, the patient appeared extremely undernourished and emaciated, weighing but 82 pounds (37.19 Kg.), whereas one year previously she had weighed 130 pounds (158.96 Kg.). The skin at first seemed uniformly sunburned, but then became discolored, thickened and exfoliated in sharply demarcated areas over the dorsa of the hands, wrists, face and upper anterior portion of the chest. Numerous white patches were present on the mucous membrane of the nose; the nasal septum was intact. The gums were completely edentulous, and the tongue showed a "bald spot" and had a bright red, beefy margin. White mucous patches were also present on the floor of the mouth, palate and inner aspects of the lips and cheeks. The patient salivated to a marked degree.

Neurologic examination revealed an extremely uncooperative patient having frequent opisthotonic spasms. Sensory examination was unreliable. Vision was apparently normal, but there were slight sclerotic changes in the fundi. Extraocular movements were well performed, and there was no nystagmus. The pupils were round and regular, but the left was larger than the right; both reacted sluggishly to light and in accommodation. The motor part of the fifth cranial nerve was normal, but sensory perception on the face was extremely diminished.

Wasting and atrophy were marked in the facial musculature, and frequent twitches and tremors occurred in it; they were more marked in the lower part of the face. Hearing as well as the motor functions of the ninth and tenth cranial nerves were apparently normal. Marked wasting was present in the sternocleidomastoid and trapezius muscles. Fine and coarse tremors were present in the tongue. All the deep reflexes were hyperative except the tendo achillis, which was absent bilaterally, but the patient had marked foot drop with shortening of the cord of both heels. The corneal reflexes were present; the pharyngeal reflexes diminished, and the epigastric and hypogastric reflexes absent. The plantar responses were flexor in type, but the absence of the Babinski reflexes might be explained by the marked bilateral drop of the toe. The Kernig test was negative, as were the Oppenheim, Shaefer, Gordon, Mendel-Bechterew and Rossolimo tests. It was impossible to test thoroughly the motility, posture and gait because the patient was bedridden, but there was marked weakness in extension of both hands and a bilateral "main en griffe"; a spastic quadriplegia was present, but the legs were more involved than the arms. Twitchings, frequently of a fibrillary nature, as well as fine and coarse tremors, were visible in the face, arms, hands, fingers, legs and toes. Movements of coordination were made extremely clumsily. There did not seem to be any disturbance of speech; writing could not be tested. Superficial and deep sensation were apparently extremely diminished over the entire body in all sensory modalities. Only occasionally would the patient cry out when the calves were squeezed very tightly.

The patient was confused mentally and showed much random spontaneous activity with her extremities; some purposeful motor activity, however, could be elicited. She frequently picked at her skin and at the bedclothes. The behavior was somewhat negativistic. Numerous laughing and crying spells occurred, which seemed to be delirious. She spoke spontaneously and occasionally in response to questions, but her speech was somewhat overproductive, rambling, incoherent and frequently rather irrelevant, and approached the word-hash variety. There was occasional echolalia. She showed affective disharmony, and her mood was extremely labile in that she could be seen happy, depressed, apprehensive, irritable and silly within an interval of a very few minutes. She had numerous delusional ideas concerning death, hell and heaven, but these were vague, indefinite and unsystematized. There was no depersonalization. Orientation as to place and person was intact, but was impaired as to time. Intelligence appeared to be a little under normal; insight was completely lacking. She had frequent hallucinations, often of a terrifying somatic nature. Memory for recent and remote events was entirely absent, but she occasionally gave her name and those of some of her relatives on questioning.

Laboratory Findings.—Blood: red cells, 5,000,000; Kahn and Wassermann tests negative; nonprotein nitrogen, 27 mg.; blood sugar, 106 mg. per hundred cubic centimeters. Urine (preceding the cystitis): normal. Cerebrospinal fluid: xanthochromic; Wassermann test negative; colloidal benzoin test, 0024443222. Stools: black; unformed; no gross blood; intermittent presence of occult blood; no ova or parasites.

Course.—Three days after admission to the hospital, there developed marked diarrhea and urinary retention. The patient was catheterized on several occasions and developed a severe cystitis; an inlying catheter was inserted, and the amount of pus in the urine diminished markedly after a few days. She was given by tube a diet rich in vitamins, supplemented with 2 tablespoonfuls of vitavose daily, but this produced no improvement in the condition. In addition, clyses of dextrose

and saline solution were given. When, after sixteen days of this dietary regimen, the patient failed to show any improvement, a daily parenteral administration of the vitamin B concentrate of Block and Cowgill[11] was begun. Within three days after this form of therapy was started the appetite improved markedly. The lesions in the mouth and skin began to disappear on the fifth day and were practically healed by the seventh day. The lesions on the skin were strikingly improved; the diarrhea decreased in severity, and the patient gained 2 pounds (907.2 Gm.) in weight. Otherwise, the condition remained unchanged. Soon after, however, signs of pneumonia developed in the right lung, and in spite of supportive treatment she died on July 25, 1932, one month after admission to the hospital.

Necropsy.—The examination was begun five hours and thirty-five minutes post mortem. The important observations were: The body was poorly nourished and poorly developed, measuring 162 cm. (64 inches) in length and weighing 37.7 Kg. (83 pounds). Fine white scales were present on the skin of the upper part of the thorax anteriorly, at the root of the neck and on the extensor surfaces of both forearms, being particularly prominent about the wrists. The skin in these regions had a thickened, leathery consistence and a brown color. A small, superficial decubitus, 2 cm. in diameter, was present over the sacrum. The musculature of the upper extremities and thighs was atrophic. The lower extremities were in foot-drop position. The mucous membranes of the lips were somewhat cyanotic; those of the buccal surfaces and pharynx were free from ulcerations and other abnormalities, as were also the gingivae and tongue. Within the pelvic cavity were dense adhesions which bound the posterior surface of the uterus and the amputated stump of the right fallopian tube to the rectum. Adhesions completely obliterated the right pleural cavity. Zones of pneumonic consolidation were present in all three lobes of the right lung, and a few similar though smaller patches were also present in both lobes of the left lung. Both kidneys were swollen and soft; the left contained three or four scattered abscesses in the cortex; the right was apparently free from abscesses. The renal pelves were not dilated, but they contained purulent fluid. Both ureters were dilated, slightly tortuous and contained similar purulent fluid. The urinary bladder had a capacity of about 200 cc. and a greatly thickened wall with necrotic and hemorrhagic mucosa; it was filled with thick, frankly purulent urine. The mucosa of the entire gastro-intestinal tract was pale and intact.

The brain and spinal cord, the right sympathetic nerve chain and portions of the vagus, phrenic, median, lateral femoral cutaneous, obturator, sciatic and superficial peroneal nerves, as well as portions of the brachial and lumbar plexuses, were removed for examination. These tissues were sectioned on removal from the body and blocks fixed in 96 per cent alcohol, in a diluted solution of neutral formaldehyde (U. S. P. 1:10) and in Mueller's solution. In addition to the staining technic employed in studying the material in case 1, preparations were also stained by the Marchi and Kulschitzky methods.

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11. This was a concentrate of the antineuritic vitamin (B_1) prepared from rice polishing by adsorption on and elution from Fuller's earth. The Fuller's earth elutate was further purified by the carbon tetrachloride-oxidation technic of Block and Cowgill (Block, R. J.; Cowgill, G. R., and Klotz, B. H.: J. Biol. Chem. **94**:765, 1932; **96**:127, 1932). The latter procedure made the vitamin B_1 concentrate suitable for parenteral administration.

The cerebral meninges were thin and translucent on macroscopic examination. The cerebrum was uniformly and symmetrically atrophic, but the sulci were not enlarged. On frontal section the cortical gray matter appeared to be well demarcated from the subcortical white matter. No lesions were seen in the mamillary bodies or in the periventricular gray matter. The ventricles were not dilated, and their ependymal lining was smooth. The spinal meninges and the cord itself were entirely normal externally and on section. All the cranial, spinal and peripheral nerves were normal in appearance and consistence.

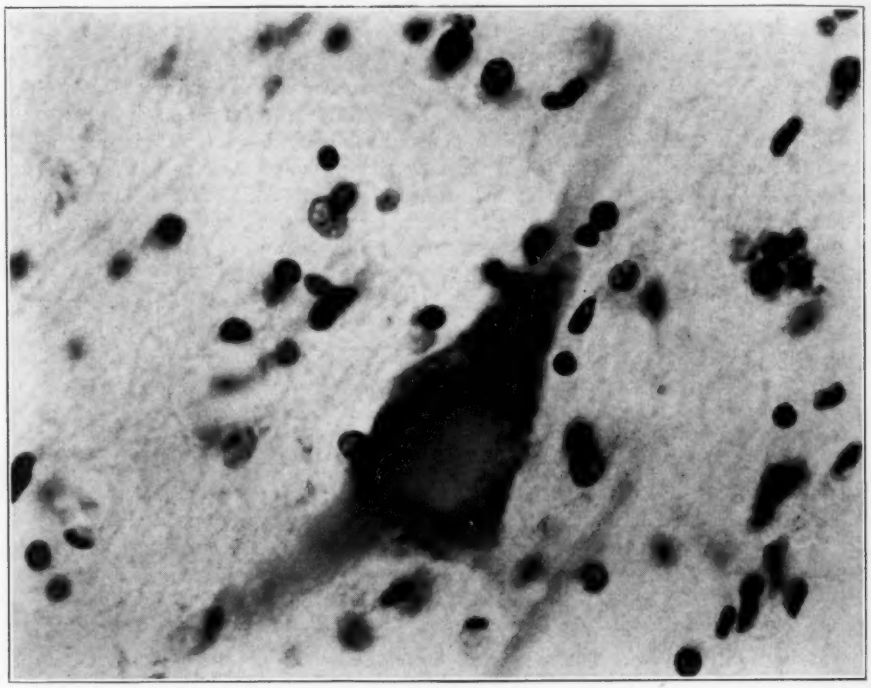

Fig. 1 (case 1).—Photomicrograph of cell in the anterior horn of the spinal cord, showing the eccentric position of the nucleus and the hyaline cytoplasm. Nissl method; × 800.

On microscopic examination, the skin of the upper part of the thorax anteriorly showed a pronounced desquamation of the superficial layers of squamous cells, leaving a thin epidermis composed almost entirely of basal cells. These showed striking evidence of regeneration and proliferative activity by the presence of numerous mitotic figures. The epithelial covering of the tongue was intact, but in the basal cell layer were numerous cells in mitosis. Such cells were also frequently encountered in the esophageal mucosa. The zones in the lungs which appeared consolidated contained an exudate of polymorphonuclear leukocytes and large mononuclear phagocytic cells. Red blood cells in large numbers were present in many of the pulmonary alveoli. The uriniferous tubules of both kidneys contained large numbers of leukocytes which often infiltrated the interstitial tissue. There was extensive necrosis of the renal parenchyma. The mucosa of the renal

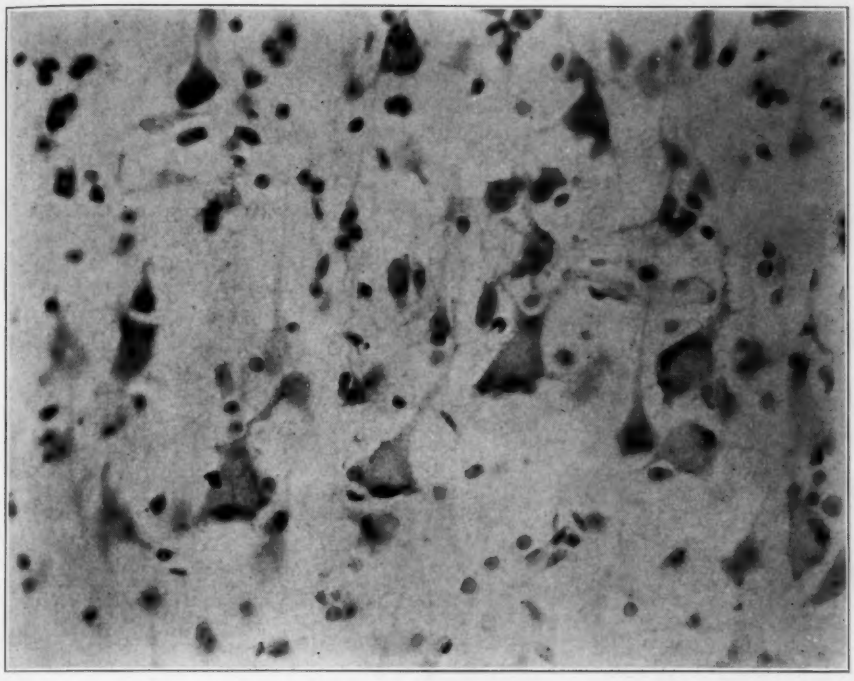

Fig. 2 (case 3).—Photomicrograph of the motor cortex, showing the "axonal" reaction in the giant cells of Betz. Nissl method; × 375.

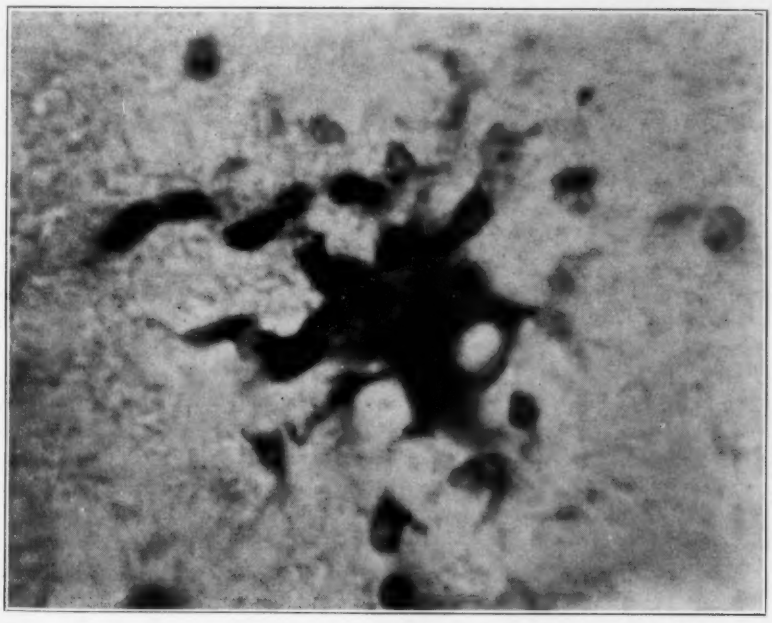

Fig. 3 (case 3).—Glia rosette in the posterior column of the spinal cord. Nissl method; × 800.

pelvis was desquamated over large areas, and the submucosa was infiltrated with numerous polymorphonuclear leukocytes. The mucosa of the urinary bladder was necrotic; the submucosa contained large numbers of leukocytes and edema; all the constituents of the exudative process extended into the muscle layers of the bladder. The gastric mucosa was intact and contained the usual complement of chief and parietal cells. The duodenal mucosa just beyond the pylorus was desquamated, and the underlying submucosa was thickened and infiltrated with collections of shrunken, hyperchromatic mononuclear cells. This lesion represented a chronic ulcer. In one or two places the mucosa lining the large and small intestines was ulcerated, and the submucosa was thickened and infiltrated with small, darkly stained, mononuclear cells. An occasional cell in the mucosa was undergoing mitotic division. There was a slight tendency for the cells of the mucosa to undergo metaplastic change with the formation of a pseudostratified squamous epithelium.

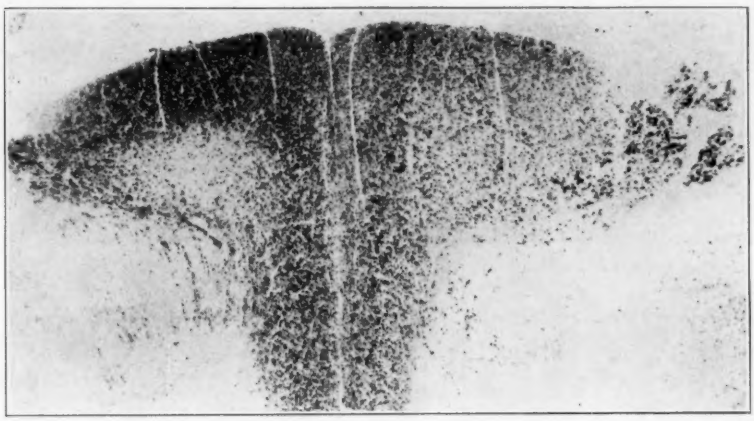

Fig. 4 (case 3).—Photomicrograph of the posterior columns of the spinal cord. Note the great extent of destruction of the medullary sheaths in the fasciculi graciles and cuneati. Marchi method. Reduced from a magnification of × 20.

The absence of cellular exudation in the cerebral meninges was confirmed by microscopic examination. A normal picture was presented by the cerebral cortical cyto-architecture, but changes of a characteristic type were present within the nerve cells of the cortex. These changes were: swelling of the cells, loss of the Nissl apparatus, a hyaline appearance of the cytoplasm and eccentric position of the nucleus. They were of the variety usually called "axonal" change and were present to the most marked degree in the giant cells of the motor cortex (fig. 2). Similar changes were seen in the cells of the nuclei dentati of the cerebellum, in those of the nucleus funiculi gracilis and of the nucleus funiculi cuneati of the medulla and in the cells of the nuclei radicis spinalis and anterior horns of the spinal cord. Many of the pontile nuclei also contained cells with swollen cytoplasm of a homogeneous glassy appearance.

The cortex of the cornu ammonis formation contained cells which were undergoing ischemic, necrobiotic changes. Other nerve cells had entirely disappeared. Some were shrunken and hyperchromatic and were surrounded by pericellular incrustations. The Purkinje cells of the cerebellar cortex were similarly altered.

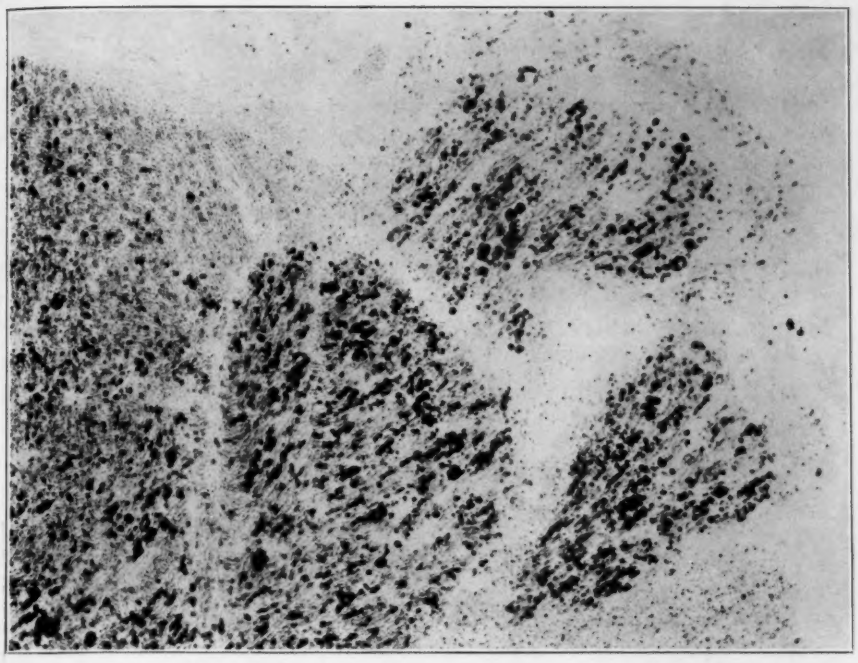

Fig. 5 (case 3).—Photomicrograph of the posterior nerve root and posterior column of the spinal cord, showing extensive destruction of the medullary sheaths. Marchi method; × 95.

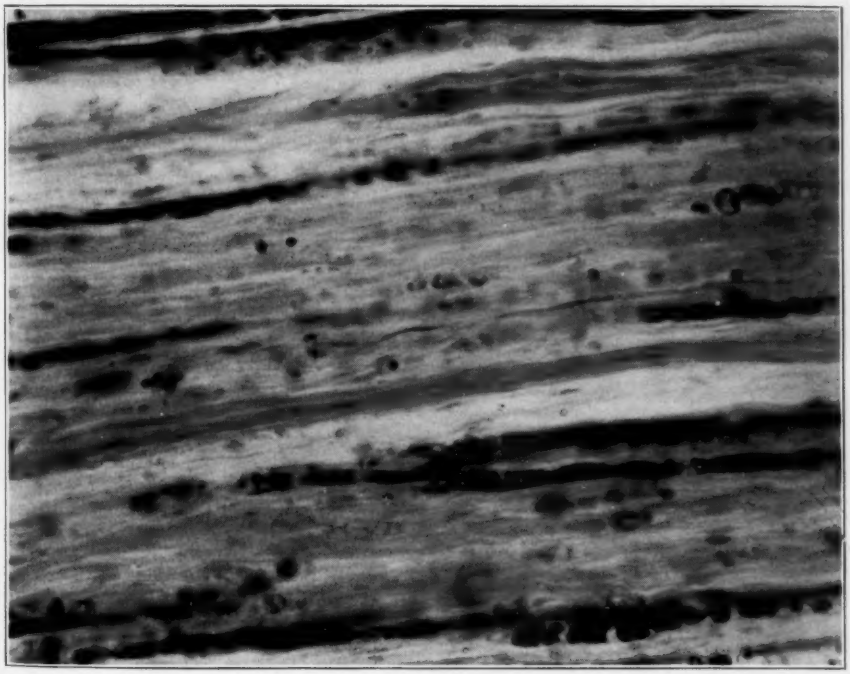

Fig. 6 (case 3).—Photomicrograph of the sciatic nerve. Note the great degree of demyelinization. Spielmeyer's method; × 375.

It proved impossible to find vascular changes of any kind in the cerebrum. In view of the history of chronic alcoholism, careful examination was made of the periventricular regions, the mamillary bodies, the floor of the fourth ventricle and the zone around the aqueduct of Sylvius, but no changes of a proliferative or hemorrhagic nature were encountered. Equally fruitless was the search for lesions in microscopic preparations stained by the Marchi and Kulschitzky methods and with sudan III.

By contrast, the spinal cord disclosed striking lesions in the preparations stained by nearly all the histologic methods. In the Nissl preparations a diffuse increase of the neuroglial processes in the dorsal columns and to a less extent, in the lateral and anterior motor tracts was seen. These processes formed an intricate network in which were caught many purplish globules of disintegrating myelin. In the same fiber tracts were present large numbers of protoplasmic astrocytes, glia phagocytes and glia rosettes (fig. 3). The changes in the cells of the anterior

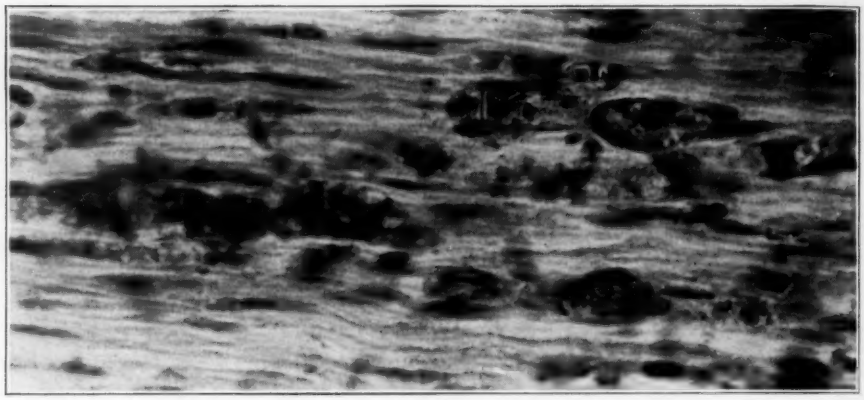

Fig. 7 (case 3).—Sciatic nerve, showing fatty change in the medullary sheaths. Sudan III stain; × 550.

horns have already been described. In the Marchi preparations the funiculi gracilis and cuneati were completely destroyed (fig. 4). These tracts, in preparations stained with sudan III, contained only a few scattered red granules, and the Spielmeyer preparations also gave but slight indication of the severity of the destructive lesion. By no means did the destruction of the medullary sheaths confine itself to the posterior columns (funiculi graciles and cuneati), for, although less extensive, it was present as well in nearly every fiber tract of the spinal cord. Striking changes were also seen in both the anterior and posterior nerve roots of the cord. The destruction of the medullary sheaths was most marked at the points of entrance of the posterior roots into the cord and was best seen in the Marchi preparations (fig. 5).

Extensive destruction of the medullary sheaths was seen in every one of the peripheral nerves removed for microscopic examination. In some of the nerves, however, the process was more extensive than in others. On the whole, it would seem that the distal nerves were more extensively involved, and that they were injured for a longer time than the more proximal nerves. The latter appeared to be true from the fact that the demyelinization of the distal nerves could be shown

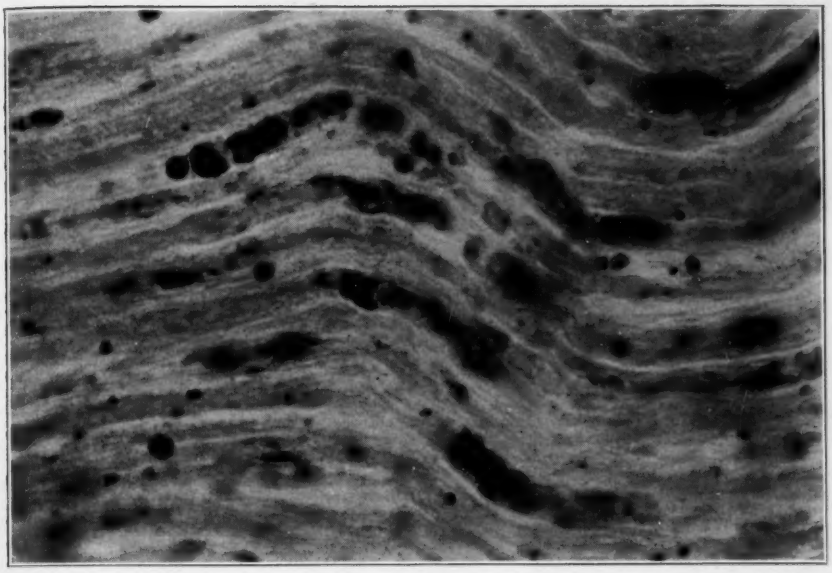

Fig. 8 (case 3).—Vagus nerve, showing fatty change in the medullary sheaths. Marchi method; × 340.

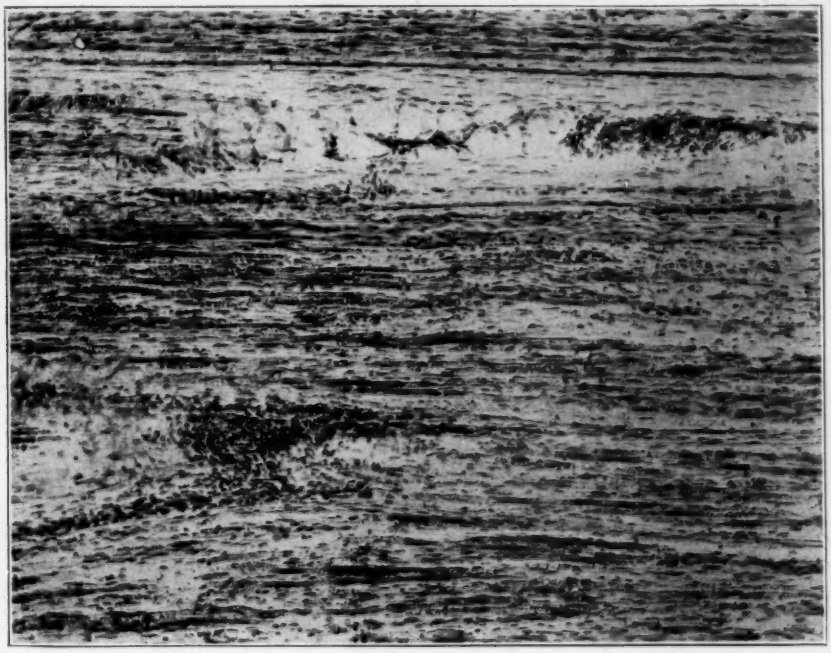

Fig. 9 (case 3).—Superficial peroneal nerve, showing the atrophic funiculi, large mononuclear cells with phagocytosed lipoids, and perineurial fibroblastic proliferation. Sudan III stain with hematoxylin counterstain; × 95.

only in Spielmeyer and sudan III preparations (figs. 6 and 7), whereas this process in the proximal nerves could be shown best in the Marchi preparations (fig. 8). In the distal nerves (superficial peroneal) fat granules were seen not only within the funiculi, but also between them, outside the endoneurium. There was much phagocytosis of lipoids by large mononuclear cells, and the atrophic funiculi were replaced by connective tissue which was quite cellular (fig. 9). In the Spielmeyer preparations many fragmented medullary sheaths were seen, as well as numerous "balloons" of degenerated myelin. Owing to their complete disintegration many sheaths failed to stain at all by this method.

Comment.—This patient presented the classic triad of symptoms in pellagra—dermatitis, diarrhea and dementia. Early in the course of her stay at the hospital, before the diarrhea appeared, she was seen by Dr. Alfred G. Nadler, dermatologist to the New Haven Hospital, who diagnosed the condition as pellagra on the basis of the lesions on the skin and particularly the tongue. In addition to this characteristic clinical picture, certain of the anatomic findings, which will be discussed later, indicate that the condition was unquestionably one of pellagra.

It proved impossible to feed this patient by spoon; tube feedings of a diet rich in vitamins, supplemented with 2 tablespoonfuls of vitavose daily, produced no improvement in the patient's condition. It therefore seemed evident that either some "intrinsic factor" (such as the substance demonstrated by Strauss and Castle[12] to be present in normal gastric juice and necessary for the prevention of pernicious anemia) was lacking, or that the mechanism for the absorption of essential substances was impaired. The vitamin B_1 concentrate of Block and Cowgill was then administered once daily by subcutaneous injection, and remarkable improvement in appetite and in the condition of the cutaneous lesions soon appeared. This illustrates the fact that the administration by mouth of large amounts of vitamins for a long period (sixteen days) may not be effective. The prompt disappearance of the oral and cutaneous lesions and the recovery of appetite following the injection of vitamin B_1 concentrate demonstrates that it may be possible to supply some essental extrinsic factors of diet parenterally when prolonged administration by mouth has failed. It thus appears that there must have been some deficiency in this patient either in an unknown "intrinsic factor" or in the capacity of absorption of dietary essentials from the stomach or intestine.

GENERAL COMMENT

It is agreed by nearly every one who has studied the anatomic changes in pellagra that there are no characteristic lesions produced by this disease except in the nervous system. In an excellent review of

12. Strauss, M. B., and Castle, W. B.: The Nature of the Extrinsic Factor of the Deficiency State in Pernicious Anemia and in Related Macrocytic Anemias, New England J. Med. **207**:55, 1932.

the whole subject of pellagra published by Raubitschek[13] in 1915, the most significant changes that are emphasized are those occurring in nerve cells, particularly in the giant cells of Betz, consisting of the "axonal" type of change or the *primäre Zellreizung* of Nissl. Changes of a similar nature have been found by Babes and Sion, Anderson and Spiller,[14] Ostertag,[15] Winkelman[16] and Pentschew[17] in the motor cells of the anterior horns and in the cells of Clark's column of the spinal cord. It must be emphasized that these cellular changes, as is well known, are not found exclusively in pellagra, but are "characteristic" of this condition only so far as they occur in it with striking regularity. The two cases presented in this communication which came to necropsy showed the "axonal" type of cellular change in these locations of predilection.

Certain other frequent though inconstant changes occur in the nervous system in this condition. Among them are deposits of lipoid in nerve cells (case 1). This form of change, however, is seen so frequently in so great a variety of pathologic conditions that it cannot be properly considered as a lesion characteristic of pellagra. It is rather to be considered as a manifestation of regressive changes in nerve parenchyma, regardless of etiology. Another change frequently encountered is the hyalinization of capillaries and precapillaries in the superficial laminae of the cerebral cortex (case 1), but the capillaries and precapillaries of the nervous system react with hyalinization to a large variety of injurious agents. The changes of an ischemic nature seen in the cornu ammonis (case 3) have apparently been described only once before in pellagra (Pentschew) and are probably to be considered of secondary significance.

Of far greater import than any of these inconstant findings are the changes in the fiber tracts of the spinal cord. These were apparently first described by Bouchard[18] in 1865 and by Tuczek, Sandwith,[19]

13. Raubitschek, H.: Pathologie, Entstehungsweise und Ursachen der Pellagra, Ergebn. d. allg. Path. u. path. Anat., Abt. 1 **18**:662, 1915.

14. Anderson, P. V., and Spiller, W. G.: Pellagra, with a Report of Two Cases with Necropsy, Am. J. M. Sc. **141**:94, 1911.

15. Ostertag, B.: Zur Pathologie der akuten Pellagrapsychosen (mit Demonstration), Zentralbl. f. d. ges. Neurol. u. Psychiat. **40**:127, 1925.

16. Winkelman, N. W.: Beiträge zur Neurohistopathologie der Pellagra, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:38, 1926.

17. Pentschew, A.: Ueber die Histopathologie des Zentralnervensystems bei der Psychosis pellagrosa, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:17, 1928.

18. Bouchard, M.: Etude d'anatomie pathologique sur un cas de pellagre; lésions de la moelle épinière, du coeur et du foie, Compt. rend. Soc. de biol. **1**:51, 1865.

19. Sandwith, F. M.: Three Fatal Cases of Pellagra, with Examination of the Spinal Cords, J. Path. & Bact. **7**:460, 1901.

Singer and Pollock,[20] Winkelman, Pentschew and many others subsequently. They consist of degeneration of the medullary sheaths of the posterior columns and frequently also of the crossed and uncrossed pyramidal tracts. The degenerated medullary sheaths are ultimately replaced by gliosis. In essence, the lesions in the spinal cord are identical with those found in our cases 1 and 3. These changes are not found, of course, in every case of pellagra, but occur with sufficient frequency in this condition to be considered an integral part of the pathologic picture. Tuczek found them in all four of his patients with pellagra who came to necropsy. Winkelman, however, found them in only one of his four patients. In the seven cases of Pentschew they were completely absent in one and present to a minimal degree in two others and to a marked degree in four. They were considered by the last-named writer to be analogous to the subacute degeneration of the cord of pernicious anemia. He believed that they do not constitute a "primary system disease of the spinal cord" and "have nothing to do with the unknown cause of pellagra, but are produced rather by the nutritional disturbances of unknown and nonspecific nature which accompany this disease" (sic!). Pentschew still speaks of a mysterious "toxin" as the etiologic agent of pellagra.

Tuczek, Sandwith and Singer and Pollock described degeneration of the posterior nerve roots, and less frequently also of the anterior roots, of the spinal cord. Sandwith even stated that his pathologist, Dr. Batten, believed that the sclerosis of the posterior columns of the spinal cord in his two cases was of root origin, being secondary to the degeneration of the posterior nerve roots. The degenerative changes seen in both the posterior roots and columns in our case 3 might be explained by this attractive hypothesis. It is interesting to note, however, that the first case of Anderson and Spiller showed diffuse degeneration in the posterior and anterolateral columns of the spinal cord without any changes in either the anterior or posterior nerve roots.

With regard to the degenerative changes in the peripheral nerves of our case 3, it must be stated that Righetti [21] alone has presented anatomic evidence of "polyneuritis" in a case of pellagra. What the incidence of this condition in pellagra really is cannot be stated with any degree of accuracy as the peripheral nerves have apparently been but rarely examined at necropsy.

Since the work of Goldberger, who proved that pellagra could be relieved by a diet rich in vitamins, but little serious doubt is entertained concerning the etiologic rôle which these substances play in this disease.

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20. Singer, H. D., and Pollock, L. J.: The Histopathology of the Nervous System in Pellagra, Arch. Int. Med. **11**:565 (June) 1913.

21. Righetti, R.: Polineurite radicolare in un caso di psicosi pellagrosa, Riv. di pat. nerv. **4**:433, 1899.

Persons may be deprived of dietary essentials by lack of funds to purchase them, by a loss of appetite which interferes with their ingestion or, when such substances are ingested, by some disturbance in the gastro-intestinal function which prevents their assimilation. A factor responsible for at least the two last-mentioned possibilities is the state of chronic alcoholism present in our three cases. All three patients lost their appetites directly as the result of alcoholism. In the third patient the disease progressed to such a degree that there was also a disturbance in gastro-intestinal function which apparently interfered with the assimilation of vitamins fed by stomach tube.

SUMMARY

Clinical symptoms and signs were presented by the three patients who form the subject of this communication which in two were strongly suggestive, and in one quite characteristic of the condition called pellagra. This diagnosis was confirmed by the anatomic findings in the nervous systems of two of the patients who came to necropsy. It was further confirmed by the fact that two of the patients properly treated responded in a strikingly favorable manner to vitamin therapy. One of the patients so treated ultimately recovered almost completely; the other died of intercurrent pneumonia after showing marked improvement; the third patient, who was inadequately treated, showed a steady progression of the disease, from which he died. The observation made was that a patient may respond favorably to vitamin therapy administered parenterally after failing to respond at all to the administration of vitamins by mouth. Finally, it was suggested that chronic alcoholism, by producing a loss of appetite or an interference with the assimilation of ingested vitamins, may have brought about the pellagrous condition in all three patients.

MYELOPATHIA ALCOHOLICA ASSOCIATED WITH ENCEPHALOPATHIA ALCOHOLICA

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Recent studies in encephalopathia alcoholica by Schilder and myself [1] showed five different clinical pictures, depending on whether the most prominent features were: (1) clouding of the consciousness with changing rigidities in the limbs, (2) cerebellar disturbances, (3) catatonia-like condition, (4) prolonged delirium or (5) polyneuritic features. In the clinical study the symptoms associated with cerebral, cerebellar and brain stem disturbances were emphasized, while those associated with lesions of the spinal cord or of the peripehral nerves were mentioned only in passing. Postmortem neuropathologic studies were made in seven of the cases with findings that correlated with the clinical groupings. The lesions always occurred in parts of the central nervous system adjacent to the spinal fluid. It was essentially a reactive, productive, invasive ependymitis of all the ventricular surfaces, and a marginal gliosis of all the surfaces of the brain and brain stem with an underlying proliferative hemorrhagic disturbance of the vascular bed which invaded the nervous system from the pial and ventricular surfaces, especially about the ventricles, where the lesion tended specifically to elect the periventricular gray masses with vegetative functions, such as the vital nuclei and the mamillary bodies of the third ventricle. In one case (case 13) the spinal cord was also studied and showed a lesion of comparable distribution which appeared to be simply an extension of the lesion from the brain stem (fig. 15 of previous paper). In the spinal cord "The sacral level showed . . . gliosis of the central canal and marginal gliosis . . ." and "an increase in the perivascular spaces about the walls of the vessels in the gray matter between the anterior and posterior horns. The lower thoracic levels showed numerous small hemorrhages around Clarke's nucleus, with congestion in the nucleus and chromatolysis of the large nuclear nerve cells. At the lower cervical level . . . where the lateral horns were evident,

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From the Research Department of the Psychiatric Division of Bellevue Hospital.

1. Bender, Lauretta, and Schilder, Paul: Encephalopathia Alcoholica: (Polio-Encephalitis Hemorrhagica Superior of Wernicke), Arch. Neurol. & Psychiat. **29**:990 (May) 1933.

there were rather severe hemorrhages . . . around the branches of the anterior central arteries. . . . At the lower end of the medulla, just where the central canal opened, there was a severe gliosis along the slit, invading toward the nucleus of the twelfth nerve." This case belongs to the group with the catatonia-like picture, with dissociation in thinking, pointing, grasping, asynergia, changing rigidities, dissociation in motility, increased reactions to pain and moderate pupillary disturbances. The symptomatology of the spinal cord was not prominent unless one can ascribe some of the profound vegetative disturbances to the lesions in vegetative centers of the spinal cord. This subject will be discussed later.

Changes in the spinal cord in chronic alcoholism have long been reported in the literature. But in the past the emphasis has been placed on the funicular or tract degeneration, especially in the dorsal and lateral columns, and so the condition has been compared with tabes dorsalis of syphilitic etiology and combined system disease in pernicious anemia, and it has been suggestively called alcoholic pseudotabes or alcoholic pseudocombined system disease. Nonne,[2] in 1906, made this correlation and emphasized a hemorrhagic diathesis in chronic alcoholism. Since then, Ossenkopp [3] has carried the comparison further and emphasized the clinical picture of alcoholic cachexia, dysfunction of the liver, severe anemia, gastric disturbances and achylia gastrica and has shown how combined system disease is associated with such a clinical syndrome in pernicious anemia and other cachectic conditions. He has come to the conclusion that the degenerative lesions in the posterior and lateral columns and dorsal roots of the spinal cord are secondary to the cachexia in the alcoholism. In 1898, Heilbronner [4] reported changes in the spinal cords in five cases of chronic alcoholism, which were essentially myelin changes in the intramedullary parts of the posterior roots and the dorsal columns and the anterior roots. He believed they were the direct result of the action of the noxious agent on the cord and not merely secondary degeneration from the peripheral neuritis which had been recognized for some time before the lesions in the spinal cord were brought to light. He also mentioned that the motor cells of the anterior horn were pale but he did not emphasize the lesions in the gray matter. Bonhoeffer [5] reported lesions of the spinal cord in

2. Nonne, M.: Ueber Myelitis intrafunicularis und über kombinierte Strangerkrankung bei Alcoholismus chronicus. Kasuistik zur hämorrhagischen Diathese beim chronischen Alkoholismus, Monatschr. f. Psychiat. & Neurol. **20**:497, 1906.

3. Ossenkopp, G.: Atypical Myelosis with Psychosis in Chronic Alcoholism, Deutsche Ztschr. f. Nervenh. **117**:350, 1931.

4. Heilbronner, K.: Spinal Cord Changes in Alcoholic Neuritis, Monatschr. f. Neurol. & Psychiat. **4**:1, 1898.

5. Bonhoeffer, K.: Pathologic Anatomic Changes in Alcoholic Delirium, Monatschr. f. Psychiat. & Neurol. **5**:265 and 379, 1899.

twelve cases, associated with the so-called polioencephalitis haemorrhagica superior of Wernicke. He also pointed out that the characteristic lesion was a vascular disturbance in the periventricular gray matter. In the spinal cord he found degenerative changes in the pyramidal tracts and dorsal columns. He also noted proliferative and degenerative changes in the blood vessels and perivascular hemorrhages in the gray matter. Besides the myelin degeneration, Ossenkopp [5] described glial growths and ganglion cell changes in the gray matter, especially in the anterior horns and in Clarke's nuclei. Thirteen cases of chronic alcoholism with lesions of the spinal cord were reported by Homén,[6] who observed degenerative changes in the dorsal columns with diffuse changes in the fibrous septums, the blood vessels and the glial elements, especially in the posterior part of the spinal cord.

Most of the more recent studies in cerebral pathology in chronic alcoholism have not included histopathologic studies of the spinal cord. The second case of Tsiminakis [7] showed evidence of a disease of the spinal cord of the type of a transverse lesion of the midthoracic level, but the pathologic picture in the spinal cord is not described. Similar studies by Gamper,[8] Neubürger,[9] Carmichael and Stern,[10] Ohkuma [11] and Walthard and Luethy [12] do not refer to changes in the spinal cord. Oettinger and Manouelian [13] reported vacuolation in the cytoplasm of the motor cells of the spinal cord in two women with alcoholic paraplegia.

Recently in the United States the drinking of Jamaica ginger as an alcoholic beverage has produced a new form of paralysis which has been definitely related to the contaminant triorthocresyl phosphate.[14] Furthermore, the pathologic changes as well as the clinical picture are different from those found in the usual cases of chronic alcoholism and

6. Homén, E. A.: Changes in the Spinal Cord in Chronic Alcoholism, Ztschr. f. klin. Med. **49**:17, 1903.

7. Tsiminakis, Y.: Beitrag zur Pathologie der alkoholischen Erkrankungen des Zentral-Nervensystems, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **33**:24, 1931.

8. Gamper, E.: Zur Frage der Polioencephalitis haemorrhagica, Deutsche Ztschr. f. Nervenh. **102**:22, 1928.

9. Neubürger, K.: Ueber Hirnveränderungen nach Alkoholmissbrauch, Ztschr. f. d. ges. Neurol. u. Psychiat. **135**:159, 1931.

10. Carmichael, E. A., and Stern, R. O.: Korsakoff's Syndrome: Its Histopathology, Brain **54**:189, 1931.

11. Ohkuma, T.: Zur pathologischen Anatomie des chronischen Alkoholismus, Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:94, 1930.

12. Walthard, R., and Luethy, S.: Ueber Polioencephalitis haemorrhagica superior, Ztschr. f. d. ges. Neurol. u. Psychiat. **116**:404, 1926.

13. Oettinger, L., and Manouelian, Y.: Alcoholic Injuries to the Spinal Cord, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:316 (Feb. 17) 1932; abstr., J. A. M. A. **78**:1234 (April 22) 1922.

14. "Ginger Poison," Editorial, J. A. M. A. **100**:974 (March 25) 1933.

are characteristic for this poison.[15] The essential feature is a multiple neuritis, with degeneration of the myelin sheaths of the peripheral nerves and secondary retrograde degenerative changes of a moderate grade affecting the anterior horn cells of the spinal cord, especially in the lumbar and cervical levels. The lesion apparently does not involve the vascular bed or other mesodermal tissues and has no reactive features.

The clinical symptomatology in any myelopathic condition depends on what normal functions of the spinal cord are disturbed. In the simplest terms, the functions of the spinal cord may be said to be: (1) motor, in relation to body movements, a function transmitted from higher centers of the central nervous system through the pyramidal tract and the anterior horn cells; (2) sensory, in relation to the cutaneous sensibility of the body, including also kinesthetic, vibratory and related sensations, a function which is mediated by the various ascending tracts, including those of the dorsal columns and also the dorsal horns; (3) vegetative, an integrative function working through the centers in the lateral horns, and the substantia gelatinosa and related areas. In all of these functions the spinal cord acts in part as an integrative organ between the peripheral nerves, including the sympathetic system, and the brain stem and the higher brain centers. It is not possible to differentiate sharply the symptoms resulting from lesions at any one point because one knows that the pathologic process in chronic alcoholism involves all parts of the central and peripheral nervous system. However, in individual cases, the lesion is more pronounced in one part than in another, giving rise to the different clinical groups already mentioned.[1] Death is more likely to occur in cases with the more severe central lesions than in those with more severe peripheral neuritis. However, polyneuritic changes of some degree probably occur in all cases, just as myelopathic changes were found in all cases of encephalopathia that have been studied in this series of cases.

The early work of Nonne,[2] Heilbronner[4] and Bonhoeffer[5] tended to emphasize the disturbances in the motor and sensory systems associated with degenerative and fatty changes in the cells of the anterior horn and myelin sheaths of the lateral and posterior columns. It is well known that motor symptoms, especially weakness of the limbs but also reflex disturbances of the pyramidal tract and sometimes typical findings of transverse myelitis, occur in cases of chronic alcoholism, but such findings are not constant, and the motor weakness, at least, may

15. (*a*) Vonderahe, A. R.: Pathologic Changes in Paralysis Caused by Drinking Jamaica Ginger, Arch. Neurol. & Psychiat. **25**:28 (Jan.) 1931. (*b*) Smith, M. I., and Lillie, R. D.: The Histopathology of Triorthocresyl Phosphate Poisoning: Etiology of So-Called Ginger Paralysis, Arch. Neurol. & Psychiat. **26**:976 (Nov.) 1931.

well be ascribed to the neuritis or the general debilitated condition. Sensory disturbances, especially in connection with the ataxia and the loss of vibratory sense, are also well known, but may in part be related to the peripheral neuritis. In case 19, reported by Dr. Schilder and myself,[1] there is given an example of the type of sensibility disturbance which we have worked out in more detail.[16] In another series of cases, Bromberg [17] and Bromberg and Schilder [18] also studied other forms of tactual disturbances in alcoholism, but it is not yet possible to state specifically what the pathologic process is in these cases, as none of them has as yet come to autopsy. There is no doubt but that the peripheral neuritis is a prominent part of the picture in these cases. The work of Pearson [19] showing the sensibility disturbance in the form of loss of vibratory sense in old age and correlating it with arteriosclerotic changes in the vascular bed of the spinal cord is of special interest in this connection as the lesions in chronc alcoholism are also related in part to a comparable vascular distribution which accounts for a special predilection for the dorsal columns where the white matter is involved. Incidentally, the patients in this series were not senile but ranged from 35 to 52 years with an average age of 44 years.

The question of the vegetative disturbances in alcoholic encephalopathias has already been touched on in the paper by Dr. Schilder and myself. The vegetative death, emaciation, pellagroid changes in the skin, nonseptic fever and diarrhea were correlated with the electivity of the lesion for the periventricular gray vegetative centers, especially those about the third and fourth ventricle. Gamper,[8] Neubürger [9] and Ohkuma [11] also noted this distribution of the lesion, although their correlations with the clinical symptomatology were not as far-going as ours. Ossenkopp,[3] in describing myelosis in chronic alcoholism, referred to the cachexia, dysfunction of the liver, severe anemia and gastric disturbances with achylia gastrica; he compared this symptom complex with pernicious anemia and suggests that these disturbances are the cause of the combined system disease-like lesions in the spinal cord. The presence of this syndrome in chronic alcoholism has been

16. Bender, L., and Schilder, P.: Streuung und Reihenverminderung im sensiblen Abbau, Deutsche Ztschr. f. Nervenh. **129**:146, 1933.

17. Bromberg, W.: Tactual Perception in Alcoholism: Study of the Influence of Alcoholic and of Other Psychotic States on Tactual After-Effects, Arch. Neurol. & Psychiat. **28**:37 (July) 1932.

18. Bromberg, W., and Schilder, P.: On Tactile Imagination and Tactile After-Effects, J. Nerv. & Ment. Dis. **76**:1; 133, 1932.

19. Pearson, G. H. J.: Effect of Age on Vibratory Sensibility, Arch. Neurol. & Psychiat. **20**:482 (Sept.) 1928.

emphasized frequently, for example in the clinical notes of Barker.[20] Which part of the syndrome is the cause and which part is the effect, however, is still a problem for interesting speculation. Orton and I [21] correlated the lesions in the vegetative centers of the lateral horn region of the spinal cord and the vegetative symptomatology in acrodynia, pellagra and pernicious anemia. The common occurrence of pellagra in alcoholism is well recognized in this country. Klauder and Winkelman [22] reported a hundred cases. Similar reports have been made by Boggs and Padget,[23] Guthrie,[24] Hiller,[25] Rutledge [26] and others. In none of these studies is there a report of pathologic examinations of the central nervous system. However, Winkelman [27] made pathologic studies of the brain and spinal cord in other forms of pellagra, and in the later of his two papers assumed that the same types of lesions are associated with alcoholic pellagra, namely, (1) retrograde cell degeneration (Meyer's central neuritis) of the cord and brain; (2) increased lipoid content in all parts of the central nervous system, and (3) thickening and hyalinization of the blood vessels of both the brain and the spinal cord. He did not emphasize the electivity for the visceral gray centers. But he did not make a point of photosensitivity, since his hundred cases all appeared between March and October and none in the winter months.

It is possible to outline a hypothetic picture of the etiologic cycle producing this syndrome with the pathologic picture of alcoholic encephalopathy and myelopathy somewhat as follows: The chronic use of alcohol causes atrophic changes in the gastro-intestinal mucosa, interfering with the normal digestive and absorptive functions with resulting malnutrition (perhaps it might be looked on as an avitaminosis), aided by the usual inadequate food intake of the chronic drinker;

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20. Barker, L. F.: Chronic Alcoholism with Cirrhosis of the Liver and Polyneuritis, Internat. Clin. **1**:17, 1929.

21. Orton, S. T., and Bender, Lauretta: Lesions in the Lateral Horn of the Spinal Cord in Acrodynia, Pellagra and Pernicious Anemia, Bull. Neurol. Inst., New York **1**:506, 1931.

22. Klauder, J. V., and Winkelman, N. W.: Pellagra in Chronic Alcoholic Addicts, J. A. M. A. **90**:364 (Feb. 4) 1928.

23. Boggs, T. R., and Padget, P.: Pellagra, Bull. Johns Hopkins Hosp. **50**: 21, 1933.

24. Guthrie, G.: Alcoholic Pseudo-Pellagra at the Boston Psychopathic Hospital, New England J. Med. **201**:414, 1929.

25. Hiller, H.: Alcoholic Pseudo-Pellagra, J. M. Soc. New Jersey **28**:467, 1931.

26. Rutledge, E.: Pellagra in Chronic Alcoholics, Kentucky M. J. **29**:294, 1931.

27. Winkelman, N. W.: Microscopic Changes in the Nervous System in Pellagra, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:38, 1926.

the alcohol further interferes with normal renal function and gradually produces cirrhosis of the liver; the combination of these gastro-intestinal and renal dysfunctions, together with the actual alcohol itself, contributes to the noxious agent in the spinal fluid and blood stream entering the central nervous system and produces the typical lesion with a specific electivity for the vegetative gray centers, thus further interfering with the normal visceral functioning of the body as a whole, and producing a far-going cachexia, associated (under favorable circumstances) with pellagra, achylia gastrica, diarrhea, nonseptic fever and sweating; these conditions, in turn, are associated with the degeneration of the myelin sheath of the dorsal and lateral column of the spinal cord, usually called combined system disease when it is associated with the somewhat similar clinical syndrome of unknown etiology, namely, pernicious anemia. This is, of course, an elaborately interlinking hypothetic cycle, and so far is unproved. To it must also be added the psychic and motility disturbances produced by the lesions in the brain cortex and stem described by Dr. Schilder and myself.

Considerable attention has been paid to the question of the pathogenesis of the localization of the lesions in the different diseases of the central nervous system. Pearson [19] has already been quoted to show the effect of arteriosclerotic changes on the vascular bed as it has been outlined by Williamson,[28] with its resulting senile degenerative changes in the dorsal columns. Smith and Lillie [15b] have shown that the lesion resulting from the drinking of Jamaica ginger is due to the poisonous effect of the triorthocresyl phosphate on the peripheral nerves of the legs, which causes a myelin degeneration of the sheath and an ascending secondary degeneration in the anterior horn cells. Spielmeyer,[29] in an extensive study on poliomyelitis, argued that the noxious agent invades neither by the meninges nor by the blood vessels; that when these tissues are involved, it is always secondarily from the adjacent nerve tissues, and that the lesion has a predilection for motor nerve cell regions of the cortex, brain stem and spinal cord. It is thought that the neural sheaths of the olfactory nerve allow the passage of the virus from the olfactory mucous membrane into the central nervous system. It was suggested by Dr. Schilder and myself that the typical lesion in the alcoholic encephalopathies was found characteristically on the surface of the brain, brain stem and ventricles, and was therefore related primarily to the spinal fluid spaces, secondarily to the blood vascular bed which invaded the central nervous system from these surfaces and

28. Williamson, R. T.: On the Relations of Diseases of the Spinal Cord to the Distribution and Lesions of the Blood Vessels, London, H. K. Lewis, 1895; Diseases of the Spinal Cord, London, Henry Frowde, 1908.

29. Spielmeyer, W.: Zur Histopathologie und Pathogenese der Poliomyelitis, Ztschr. f. d. ges. Neurol. & Psychiat. **142**:159, 1932.

finally to the adjacent vegetative gray centers in the brain stem. For a full understanding of the distribution of the lesion in the spinal cord, it will be necessary to have an understanding of the anatomy of the cord. Like the brain and brain stems, the spinal cord is surrounded by a pial membrane and arachnoid space with spinal fluid, but unlike the brain stem, it has no ventricle, for at least in the adult the spinal canal is usually occluded by a normally developing gliosis. The only means of humoral invasion of the spinal cord is therefore through its external pial surface and through its vascular supply.

The classic work on the vascular bed of the spinal cord has been done by Dr. Williamson.[28] The thoracic aorta gives rise directly to the intercostal arteries which branch into the spinal arteries as they pass into the spinal canal with the nerve roots. Here they divide into anterior and posterior spinal branches and pass around the spinal cord, sending small peripheral vessels through the arachnoid and pia membranes by way of the septums into the margin of the spinal cord as they go to their position at the mouth of the anterior and posterior fissures of the cord; from this they pass down the cord, sending off medial branches into the fissure at regular intervals. These medial arteries are the ones that make up most of the vascular bed of the spinal cord except for the marginal vessels already mentioned, which supply mainly the lateral columns. The anterior medial vessels pass in the fissure to the region of the central canal, turn laterally and fan out over the gray horns. The posterior medial vessels supply the dorsal columns. Thus the spinal cord, from the point of view of its vascular supply, is divided into three parts: 1. The margin of the cord is supplied by small peripheral vessels entering it directly from the spinal vessels before they reach their position at the mouth of the fissures. 2. All of the gray horns are supplied from the anterior medial vessels that reach them centrally by way of the anterior fissure. 3. The dorsal columns are supplied by the posterior medial vessels of the posterior fissure. This will help one to understand the lesions to be found in the spinal cords in the cases described in this paper. Furthermore Williamson quoted Moxon[30] as saying that the main part of the blood supply is furnished through the cervical and upper dorsal regions and passes down, so that these regions receive the first and most abundant supply of the blood and the lower parts of the spinal cord have a feeble blood supply. The spinal arteries are said to be terminal and do not anastomose.

Besides the one case already reported (case 13, previous report[1]), the five following cases were studied clinically in the psychiatric division of Bellevue Hospital, and the spinal cords, brain stems and selected areas of the cerebral cerebellar cortex, as well as specimens of the

30. Moxon, R.: Lancet **1**:530, 1881; quoted by Williamson.

peripheral nerves, when these were available, were studied microscopically. All of the cases showed the lesions characteristic of encephalopathia alcoholica in the brain stem and cortices. These lesions are outlined only briefly, the main emphasis being placed on the changes in the spinal cord.

Part of the neuropathologic work was made possible by the courtesy of the Neuropathological Laboratories of the Neurological Institute of New York.

REPORT OF CASES

CASE 1.—A white woman, aged 41, was transferred from the City Hospital to the psychiatric division of Bellevue Hospital on Aug. 23, 1932, with the statement that she had been in the City Hospital for four days, the diagnosis being chronic alcoholism and alcoholic pellagra. There was a history of alcoholism for twenty years. She was reported to have been restless, in and out of bed, confused and hallucinated.

Examination.—On admission she was in a delirious state, confused, restless, misidentifying and confabulating. She said, "This is a speak-easy. I am looking for Archie. A Negro man came in smoking and tried to take me out of bed. I saw you, doctor, last night at Burke's place on Fifteenth Street. Don't knock me on the head with that hammer." She was bedridden, helpless and emaciated, with pale skin, blue sclerae and severe pellagrous lesions on the dorsal surface of both arms and hands. There were bilateral palsy of the sixth nerve, ptosis of both eyelids, complete failure of convergence, a sluggish reaction of the pupils to light, reduction in vision and atrophic changes in the optic disks. The tongue was beefy and tremulous. There was an occasional sucking reflex. Speech was slurred. There were almost constant jerking movements in all muscles, both in individual muscles and in muscle groups. There were changing rigidities in the arms, and also coarse tremors and occupational movements of the hands. There was a definite grasping reflex. There were marked tenderness in the muscles, especially in the arms, and a hyperactive response to all painful stimuli. The tendon reflexes were normal, except that the right Babinski response was positive. The heart and lungs were normal, but the liver was enlarged to just below the costal margin.

Laboratory Data.—The Wassermann reaction of the blood was negative. The spinal fluid contained no globulin and no cells; the gold colloid curve was 0111000000; the Wassermann reaction was negative. The nonprotein nitrogen of the blood was 37, and the blood sugar (fasting) was 83 mg. per hundred cubic centimeters. Liver function tests showed: bromsulphalein test, normal; direct van den Bergh test, negative, and icteric index, 12. Gastric analysis showed no free hydrochloric acid and 20 cc. of total acidity; one hour after a test meal, no free hydrochloric acid and 40 cc. of total acid. A blood count showed 3,000,000 erythrocytes, 60 per cent hemoglobin and 10,500 luekocytes, with 63 per cent polymorphonuclear cells and a color index of 1.

Course.—The condition became progressively worse in every way in the next few days. The pellagra increased in extent and severity; the patient had diarrhea and was incontinent. Mentally she was disturbed, tossing about in bed, pulling at the bed clothes, exposing herself and grasping in a semivoluntary way at everything. The sucking and grasping reflex was increased. There was a marked clouding of consciousness. The eyes were held in midposition, and when she

followed movements she would turn her head to do so. There were involuntary movements with the mouth. Speech was slurred, and there were paraphasic mistakes in naming objects. There were changing rigidities in the limbs and bilateral Hoffmann and Babinski signs. On the last day a double conjugate ocular palsy and apparent blindness were noted. There developed a terminal bronchopneumonia, and the patient died on August 31.

Autopsy.—This was performed on the same day. The anatomic diagnosis was: bronchopneumonia of the right and left lower lobes, with acute purulent tracheobronchitis; fatty changes of the liver; congestion of the suprarenal glands:

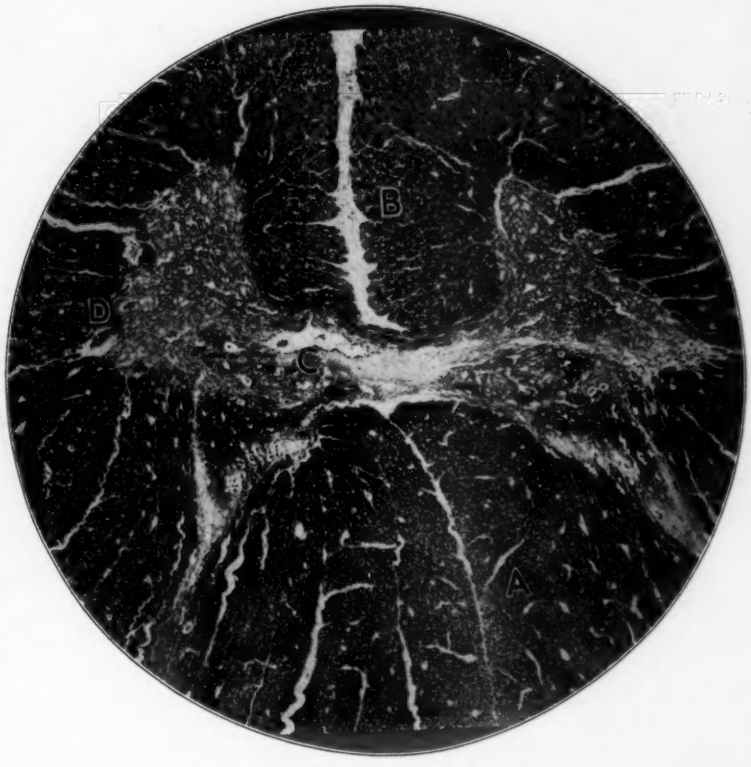

Fig. 1 (case 1).—A Weigert-Pal stain of the midthoracic level of the spinal cord. This shows the increase in perivascular and septal connective tissue in all regions with a diminution in myelin in both the dorsal (*A*) and ventral (*B*) columns, especially near the fissures. The large anterior medial vessel is seen near the central canal; it passes anterior to Clarke's nucleus (*C*) to supply the gray horn. There is considerable congestion in all parts of the gray horns with many small hemorrhages, especially about Clarke's nuclei and the lateral horns (*D*) that do not show up well in the photograph.

cyst of the left ovary; fibromyomas of the uterus, and anemia. No gross changes in the brain and spinal cord were reported.

Histopathologic Studies.—The sacral level of the spinal cord showed that the anterior and lateral funiculi and the anterior horns were fairly normal, although

there was a minimal amount of marginal gliosis, with some general congestion and proliferation of the blood vessels. However, the posterior funiculi and horns showed a striking lesion, primarily of the blood vessels. This involved mainly the vessels of the posterior fissure and the vessels of the posterior roots. There was a proliferation of all parts of the blood vessels but especially the media, and there was also an increase in the glia cells about the walls of the vessels, especially in the posterior column. There was also an increase in the capillary bed, especially in the substantia gelatinosa, where there were numerous small hemorrhages. Occasional small hemorrhages were seen in the white columns, and the

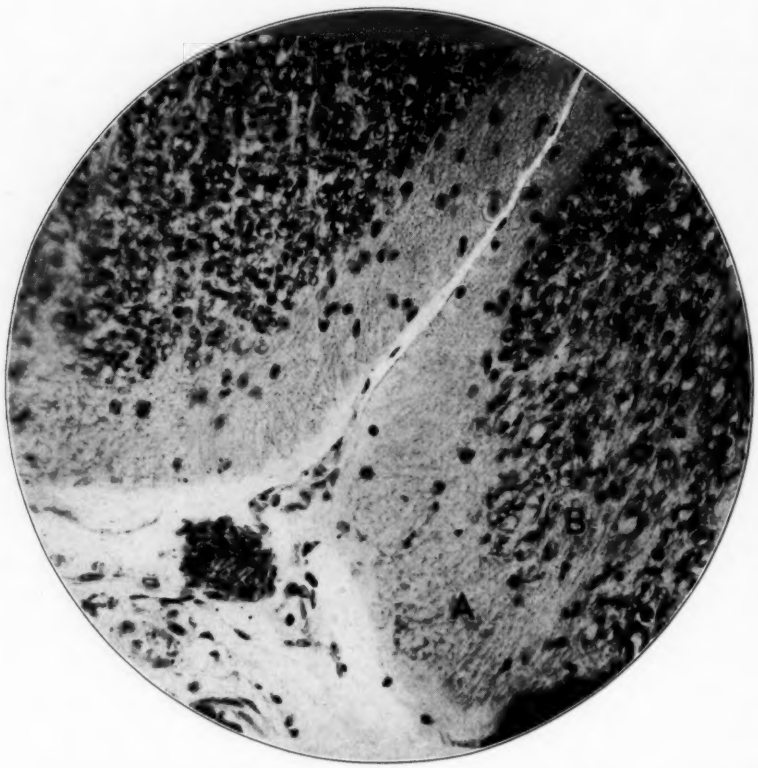

Fig. 2 (case 1).—Scarlet red stain of the periphery of the spinal cord showing a thick wall of marginal gliosis with a complete loss of myelin sheaths in this region (*A*) and a partial loss in the neighboring area (*B*).

hypertrophy of the vascular bed was also seen in the gray matter about the central canal, especially on its posterior side. Nerve cells of the anterior horn were intact by the Nissl stain.

The midthoracic region of the spinal cord showed the same lesion, but in greater severity (fig. 1). There was some apparent loss of myelin in the posterior columns with shrinkage of the cord. The vascular proliferation and hemorrhages involved both Clarke's nuclei and the lateral horns; the hemorrhages were especially marked in the latter. There was also a subarachnoid hemorrhage at this

level. The nerve cells of Clarke's nuclei were pale and distorted, while the nerve cells of the anterior horn appeared normal.

The lower cervical level of the spinal cord showed an almost specific localization of the hemorrhages in the lateral horns. There was a large vessel in the posterior fissure that showed perivascular round cell infiltration. At the upper cervical level the lesion was less severe, although there appeared to be some diffuse loss in myelin associated with an increase in perivascular fibrous tissue. The central canal showed a proliferative gliosis. The margin of the spinal cord showed a dense wall of gliosis (fig. 2) with loss of myelinated fibers and degenerative changes in the adjacent fibers.

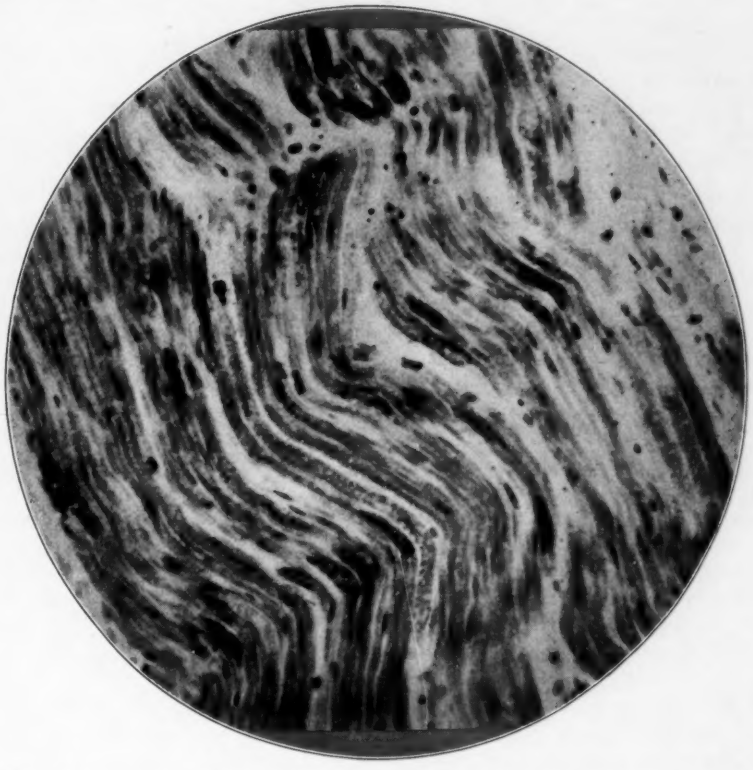

Fig. 3 (case 1).—Scarlet red stain of the sciatic nerve showing the fatty degeneration and fragmentation of the myelin sheaths.

In the pons there was the characteristic ependymal gliosis, proliferative in type, on the floor of the fourth ventricle, with some proliferative changes in the blood vessels.

In the midbrain, the aqueduct of Sylvius was considerably narrowed by a marked proliferative change in and beneath the ependyma. The posterior colliculi showed a severe marginal gliosis, with proliferating changes in the invading vessels. There was a diffuse glial invasion in all parts of the quadrigeminate bodies. Here the changes were more severe above than below the aqueduct, especially in the posterior colliculi.

The lesion in the periventricular gray matter about the third ventricle was very severe. Vascular proliferations, numerous hemorrhages and marked cellular proliferations of the glial elements were seen in the mamillary bodies, the thalamus and the hypothalamic nuclei, especially about the floor of the third ventricle. The optic nerve did not show an extensive pathologic process, although there were thickening of the blood vessels and some perivascular fibrosis with an apparent loss of myelin. The Nissl stains showed nerve cells present and intact in all parts of the thalamus and some in the mamillary bodies.

The cerebral cortex showed a marginal gliosis of the first layer and some mild congestion with proliferation of the blood vessels that invade the cortex from the pia. The nerve cells stained well by the Nissl stain. There were hemorrhages.

The sciatic nerve showed swelling, fragmentation and fatty degeneration of the myelin by the fat stains (fig. 3).

The pancreas showed congestion; the heart muscle, some fibrosis. The lungs showed bronchopneumonia and purulent tracheitis, and the liver, severe fatty infiltration.

Summary and Comment.—There were alcoholic encephalopathy with severe ependymal gliosis of all the ventricles, with the invasive gliosis most marked in the roof of the midbrain; severe hemorrhagic changes of the periventricular gray nuclei, especially those about and below the third ventricle; an alcoholic myelopathy that involved the cord, especially on the margin, and in the posterior columns and dorsal and lateral horns, including the substantia gelatinosa, Clarke's nuclei and the lateral nuclei—most severe in the thoracic region; also a gross subarachnoid hemorrhage, and fatty degeneration and fragmentation of the nerve sheaths of the sciatic nerve. The fatty changes in the liver were also worth noting.

Thus it is seen in this case that the lesions were directly related to the margin of the spinal cord and the invading vascular bed and were localized in three parts, just as the vascular bed had three parts, namely, (1) the margin of the cord; (2) the dorsal columns, with the most severe lesion nearest to the fissure or the entrance of the vessels; (3) the gray horns with the lesion entering from the center by way of the anterior median artery. Furthermore, the lesion was most severe in the region of the thoracic and cervical levels, which is the area with the freshest and richest blood supply.

The clinical picture showed the characteristic features of the encephalopathy of the first clinical group (Bender and Schilder), with clouding of the consciousness and changing rigidities, ocular findings, twitchings of the muscles and profound vegetative disturbances, including pellagra, secondary anemia, chlorhydria gastrica and diminished renal function.

The subject of peripheral neuritis will not be discussed in this paper but left for a later study.

Case 2.—A Negress, aged 52, who was born in the British West Indies and came to New York at the age of 24, had one son, aged 29. She had had a previous admission to the psychiatric service of Bellevue Hospital in April, 1917, when she was suffering from alcoholic hallucinations from which she did not immediately recover and was transferred to the Manhattan State Hospital. The same diagnosis was made there, and she was discharged at the end of a year much improved. Her son stated that he lived with her from 1920 to 1925, and that she drank whisky "all the time"; it was impossible for him to say how much. From 1923 to 1925 he noticed that she did many peculiar things, such as sprinkling

salt all over the house, praying out loud at night and talking to herself. She had the idea that he wanted to do her harm, and she made so many accusations against him that he moved away from her in 1925. He claimed that she had been unable to do any work since 1926. She continued to drink steadily. She was admitted to the psychiatric division of Bellevue Hospital on Sept. 12, 1932, as a transfer from the Harlem Hospital.

Examination.—On admission the patient walked with difficulty and complained of weakness, dizziness and dark spots before her eyes. She looked at her hands in a puzzled way and appeared to be picking threads from them. Her speech was indistinct at all times. She described visual hallucinations; she said "I saw lots of those little magic things around—like dolls or birds; they were all around and on the table, and when I went to catch one they would up and fly off; they came and ate off the table and took tea out of the cup; I didn't care; they were small (2 inches) and large (3 inches); they were black and gray and white; they didn't talk or sing; they came in the bed too, and played." She was occupational, restless, incontinent and unable to attend to her needs. She attempted to get up at night and staggered about the ward, defecating on the floor.

Physically, she was debilitated and emaciated. She was weak and unsteady on her feet and showed many restless, twitching, groping movements of the hands. The pupils were unequal, the right being greater than the left, and irregular, and they reacted poorly to light. There were bilateral arcus senilis and beginning cataracts. The tongue was atrophic, cherry red, smooth and tremulous. Speech was slurring, and there were uncertain tremors of the facial muscles. All movements of the hands were awkward, and there were changing rigidities in the arms and a grasping reflex. The tendon reflexes in the arms were normal, but the Hoffmann sign was bilaterally present. There was atrophy in the muscles of the forearms and hands and twitchings were present in the muscles. The abdominal reflexes were absent. Motor power in the legs was weak. The knee and ankle jerks were absent; the Babinski sign was negative. The muscle bellies were flabby but not tender. There was diminution in sensibility below the knee; otherwise there was delayed hyperesthesia to pain. A spinal tap gave clear fluid that showed a faintly positive reaction to the globulin test, 6 cells, an anticomplementary Wassermann reaction and a flat colloid gold curve. The Wassermann reaction of the blood was negative. From the point of view of the internal viscera, she had been complaining of gastric disturbance with pain and vomiting. She presented an atrophic tongue, tenderness over the epigastrium, a palpable liver, and a rectal fistula that contained maggots. She had a persistent and progressive diarrhea. Urinalysis showed a specific gravity of 1.020 and negative tests for globulin and dextrose. Examination of the blood showed a moderate secondary anemia, 3,200,000 erythrocytes, 55 per cent hemoglobin, and 8,200 leukocytes, with 78 per cent polymorphonuclear cells. The pulse rate ranged from 90 to 110. The temperature curve was irregular but never much elevated.

Course.—Within a week the condition progressed; the patient was delirious, confused and restless, and became rigid at times, assuming a position of opisthotonos. She became more emaciated in spite of forced feeding. Pyramidal tract signs increased; the grasping reflex became more pronounced. She was continually groping and picking at the bed clothes in an awkward way. She reacted to hallucinations, but did not respond to questions. She was unable to sit up in bed, and gradually lost the power to swallow. She died on September 24.

Autopsy.—The gross anatomic diagnosis was: congestion of the lungs and decubitus ulcers. It was reported that the brain and spinal cord appeared grossly normal.

Neuropathologic Studies.—The upper sacral and lower lumbar levels of the spinal cord showed some general congestion, which was most severe in the posterior horns, especially in the substantia gelatinosa where there were also numerous small hemorrhages. There were proliferative changes in the vessels and septums of the posterior columns, with surrounding gliosis; this was moderate. The nerve roots showed vascular proliferation, congestion and thickening of the pia. The central canal was completely obliterated by a proliferative gliosis. The nerve cells showed some distortion and loss of Nissl bodies. The cauda equina showed congestion and an increase in fibrous elements.

At the upper lumbar and lower thoracic levels (figs. 4 and 5) there was a most severe vascular disturbance, especially in the vessels that entered by way of the anterior fissure and spread out over the gray matter and, to a less extent, in the adjacent white tracts. There were proliferative changes in the blood vessels and numerous small hemorrhages. In the higher levels of the middorsal region there was some softening of the gray matter, especially about the lateral horns, with distortion of the cord and collapse and loss of some tissue. This was in part an artefact, but undoubtedly the pathologic weakness of the tissue had led to easy injury. A loosely knit glial wall was seen about the area where tissue was lost. Some atrophy and paling of nerve cells were seen, though most of those in the anterior horn were intact. Most of the white tracts were normal, though there was some apparent loss of myelin in the posterior columns. The pia was thickened.

The upper cervical level of the cord showed a more chronic type of lesion. The vessels were thickened, and there was a retraction of the glial walls about them, with large perivascular spaces into which there had been some seepage of red blood cells. In the white columns there was an increase in perivascular fibrosis and gliosis, especially in the posterior columns. There was some congestion, especially in the substantia gelatinosa. Pial thickening was marked. The nerve cells were intact.

Sections through the pons showed severe changes about the ventricle. There was a marked proliferation of the ependyma with large underlying spaces, partially filled with enormously proliferated vessels and seepage of red blood cells. The connecting capillaries were proliferated, congested and surrounded by small hemorrhagic areas. The deeper parts of the pons and the cerebellum appeared normal.

The midbrain showed a similar lesion about the aqueduct. The vessels on the surface of the posterior colliculi showed the most severe proliferative changes, with retraction of the surrounding tissue, giving a striking moth-eaten appearance to the tissue. There was a severe diffuse gliosis.

The cerebellum as a whole was in good condition. There was a congestion in the dentate nucleus with some small hemorrhages. There was also some thickening of the vessels in the white tracts with retraction of the surrounding tissue.

The third ventricle was surrounded by a most severe vascular and ependymal and glial reaction. The mamillary bodies were almost completely replaced by vascular organization and glial scarring. The vascular organization, with hemorrhage and proliferation of the glial elements, had deeply invaded the thalamus and hypothalamus. The ependymal reaction was of the reactive and invasive type.

The cerebral cortex showed some congestion, which appeared to be most severe in the temporal lobes. There were considerable pial thickening and slight marginal gliosis. The Nissl stains showed a reduction in the Nissl content and distortion of the nuclear position, especially in the large motor cells of the motor region.

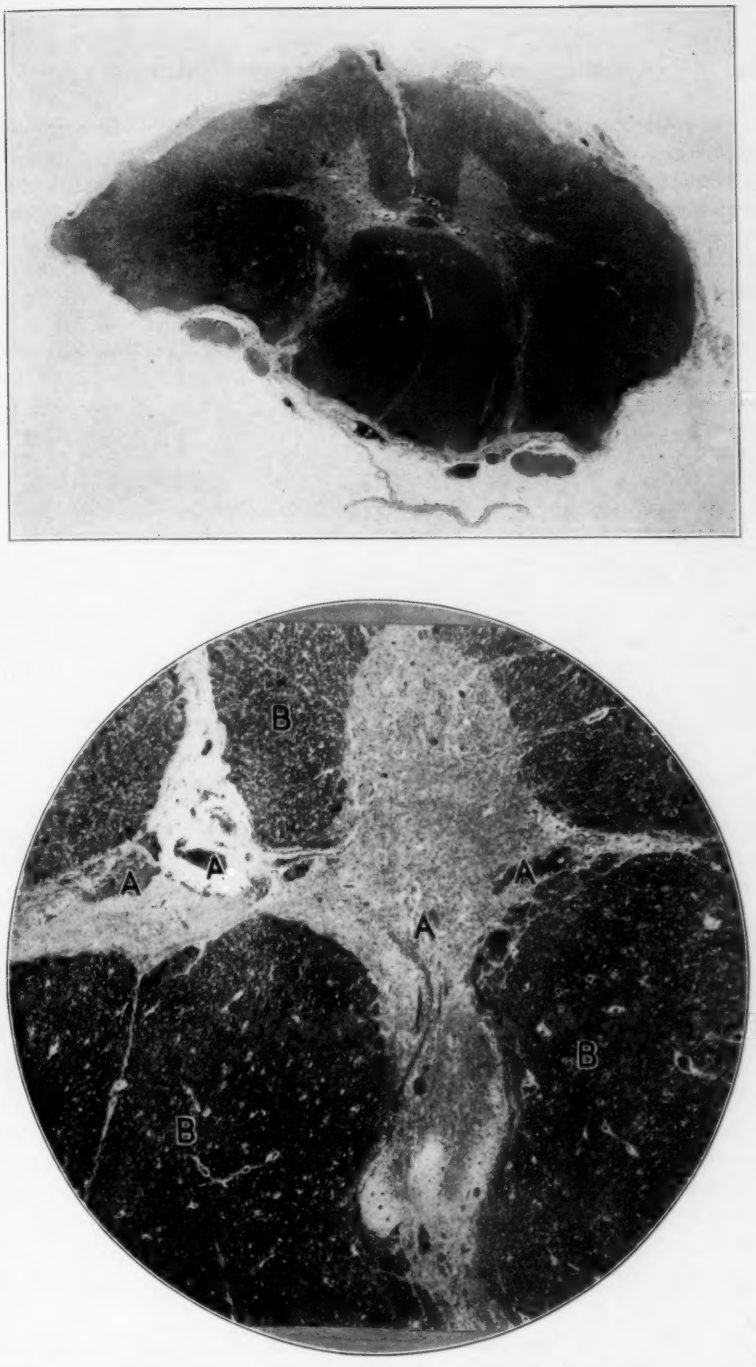

Fig. 4 (case 2).—Upper photomicrograph, a modified Loyez stain of a section of the whole cord at the thoracic level showing the marginal loss of myelin and the numerous hemorrhages; lower photomicrograph, a Weigert-Pal stain of a section at the same level, at higher magnification, showing severe hemorrhages about the anterior medial artery near the central canal (*A*), a fairly large hemorrhage near the tip of the lateral horn (*A*) and many smaller hemorrhages as well as thickening of the blood vessels in both the white (*B*) and gray (*A*) areas.

The optic nerve showed some increase in perivascular fibrosis with some diffuse increase in round cells.

Summary and Comment.—The clinical picture was one of prolonged chronic paranoid mental deterioration, with dissociation in thought processes and hallucinations culminating in a delirium with grasping and groping and changing rigidities. The case comes closest to the fourth clinical group of encephalopathia alcoholica (Bender and Schilder), with chronic delirium and acute features superimposed. There were also motor weakness and disturbances in sensibility. These symptoms may be associated with the signs of lesions of the pyramidal tract, the polyneuritis

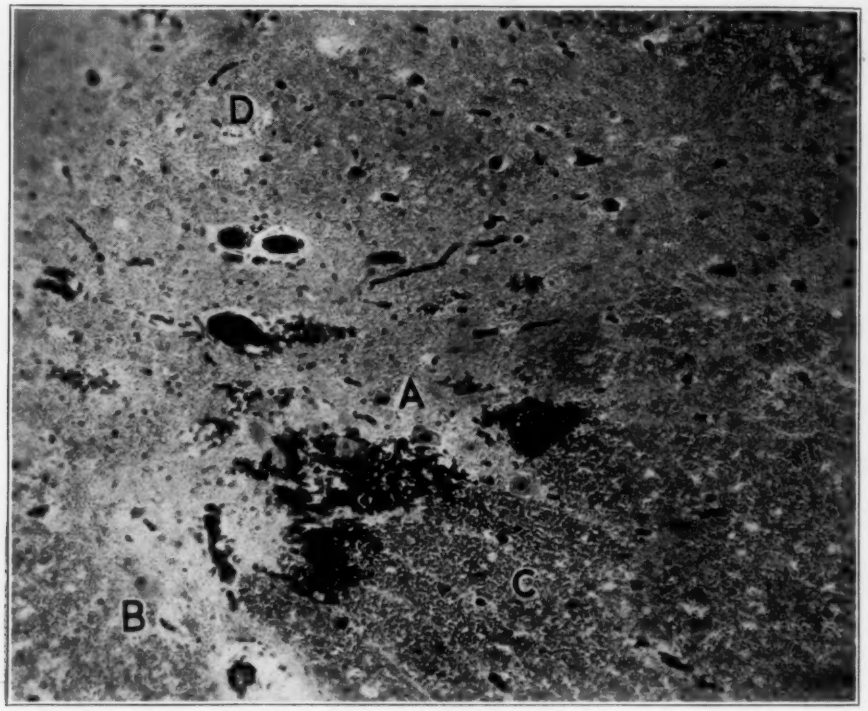

Fig. 5 (case 2).—A magnified view of an area similar to that in figure 4. It shows the severe hemorrhages about the lateral horn (*A*) with a more moderate congestion in the posterior (*B*) and anterior (*D*) horns and the lateral myelinated area (*C*). Modified Loyez stain.

or the general debility, which, in turn, may be associated with the profound vegetative disturbances.

The pathologic picture was one of severe glial and vascular encephalopathy about the ventricles, in which chronic and acute features may be distinguished. Similar lesions were found in the spinal cord, especially in the lateral and dorsal horns of the gray matter and in the posterior columns of the cervical and thoracic regions.

Case 3.—A man, aged 47, a chef, who was born in Switzerland and who had been in the United States for twenty-four years, was admitted to the medical

service of Bellevue Hospital on April 8, 1932, with a complaint of loss of power in the legs. He gave a history that he had been a heavy drinker before prohibition, but had drunk more moderately (?) since then. Two years before, he lost the power of speech for a couple of days, although he understood what was said to him. About eight weeks before admission he began to lose strength in the legs; he staggered and lost his balance; the feet gave way beneath him and he had pains all over the body. For a few days, the wife said, he had been restless and "mixed up in his head."

Examination.—The patient was well developed; the heart, lungs and abdomen were normal, except that the border of the liver was felt two fingerbreadths below the costal margin. The blood pressure was 170 systolic and 98 diastolic. He was unable to stand without support. He had a sluggish facies, with coarse tremors of the tongue, lips and hands. The pupils were normal. All tendon reflexes were hyperactive, but equal on the two sides. Touch and vibratory sensation were normal in the legs. The spinal fluid was negative for globulin, cells and the Wassermann test.

He was restless and too disturbed for the medical service and was transferred to the psychiatric division on April 21. He was then restless, semidelirious, excited and confused; he stared about the ward, clutching at the bed clothes and talking to himself, and he was inattentive. He said, "You know what is the matter—what is the trouble? It is the consommé—you know the man—Max? This is the hospital—I forget what name. I came yesterday—I came for my foot—I take too much drink—too much."

He was emaciated, with a severe watery diarrhea. He was helpless in bed, too weak to stand and unable to attend to any personal needs. He showed constant restless dissociated movements of the hands and tremors of the face. The pupils reacted sluggishly to light, and there were nystagmoid movements of the eyes. There was right facial weakness. The tongue deviated to the left, and was coated and tremulous. He rolled his head from side to side. Speech was indistinct and slurring. The abdominal reflexes were absent. There was weakness of the arms and legs, and all the tendon reflexes were hyperactive. The spinal fluid was again examined and gave negative results in all tests. The Wassermann reaction of the blood was also negative.

Course.—The condition progressed; four days later the patient was in a state of deep clouding of consciousness and did not talk. He was grasping and groping, and showed a marked grasping and sucking reflex. There was a rough tremor, and at times slight jerky or athetoid movements were noted in the arms. A support reaction was observed in the arms and to a lesser extent in the legs. There were marked changing rigidities all over the body. The reflexes were still hyperactive, and there was a bilateral Hoffmann sign; the Babinski sign was positive, more so on the left.

On the next day he was in a deep coma; the left arm was spastic and the right flaccid, and there was an external deviation of the left eye. The temperature rose to 107 F., although the lungs remained clear. The foul watery diarrhea persisted. Death occurred the same day.

Autopsy.—This was performed on the day after death and was limited to the head and spinal cord. The meninges were normal. The brain was edematous. The convolutions appeared slightly flattened. The meninges of the cord were normal. The blood vessels appeared injected, and in several places over the surface of the cord there were linear reddish streaks.

Neuropathologic Studies.—The sacral and lower lumbar levels (fig. 6) of the spinal cord were surrounded by a gross subarachnoid hemorrhage (fig. 6 *D*). There was a diffuse congestion, with multiple small hemorrhages and proliferative changes in the vessels, especially in the gray matter. Softening and glial reactions in the white matter were minimal. The nerve cells showed swelling, fatty changes and displacement of the nuclei. Nerve trunks from the cauda equina showed proliferative changes in the vessels, with congestion and hemorrhages and a diffuse fragmentation of the myelin.

Fig. 6 (case 3).—A Weigert-Pal stain of the lumbar level of the spinal cord showing the diffuse congestion of the gray matter (*A*) with numerous small hemorrhages, some extending into the white tracts (*B*). The dark mass in the arachnoid space (*D*) is a gross arachnoid hemorrhage which has arisen from the posterior medial artery of a higher level and seeped downward through the arachnoid space. On the margin of the cord (*C*) is seen the glial synctium invading the white columns with a loss of myelinated fibers.

The middle thoracic region (fig. 7) showed congestion, hemorrhages and softening, and tissue destruction. Severe hemorrhages associated with proliferative changes in the vessels occurred in the gray masses. The branches of the anterior central spinal vessels in the anterior medial fissure showed proliferation and a gross hemorrhage that had become extruded and extramedullary but sub-

arachnoid. This was apparently the source of the gross subarachnoid hemorrhage found at the lower level.

The upper thoracic region (fig. 8), including the lateral nuclei and Clarke's nuclei, showed the same lesion of a severe degree. Conspicuous proliferative and degenerative changes were seen in the vessels, and hemorrhages were severe, particularly in the gray matter and more especially in the lateral and dorsal parts, including the lateral horns, Clarke's nuclei and the substantia gelatinosa (fig. 6 *C*). There was softening beginning on the surface or margin of the

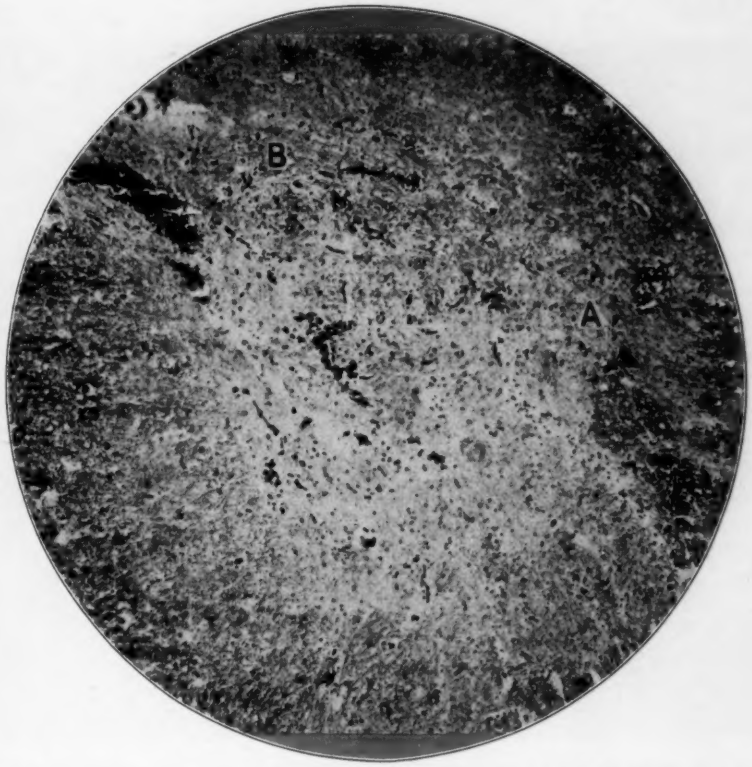

Fig. 7 (case 3).—Section through the midthoracic region including the lateral horn (*A*) and Clarke's nucleus (*B*) with hemorrhages and softening. Modified Loyez stain.

cord and invading inwardly, with a spectacular syncytium of gliosis both on the surface of the cord and invading along the fibrous trabeculae.

The middle cervical region showed a severe diffuse congestion, most marked in the gray masses, where there were numerous small hemorrhages, especially in the dorsal and lateral extensions of the horns. Some small hemorrhages were also seen in the white matter, especially in connection with the trabeculae. There was also some softening on the margin of the cord, with a reactive glial response, and a myelin stain showed loss of myelin near the margin and fragmentation of the adjacent fibers. Fat stains showed fatty changes in this region.

The lower end of the medulla showed an invasive gliosis where the central canal was opening into the fourth ventricle and hemorrhages in the surrounding gray masses, including the twelfth nuclei and the tractus solitarius and the nucleus associated with it. There was also some congestion in the olives.

The upper end of the medulla showed an ependymitis with underlying gliosis. Proliferative changes and hemorrhages were seen in the overlying velum and cerebellar lobules, and in the underlying nuclei of the sixth and eighth nerves. But there were no changes in the deeper lying seventh nuclei or in the olives. The lesion was also seen in the superficial cochlear nucleus.

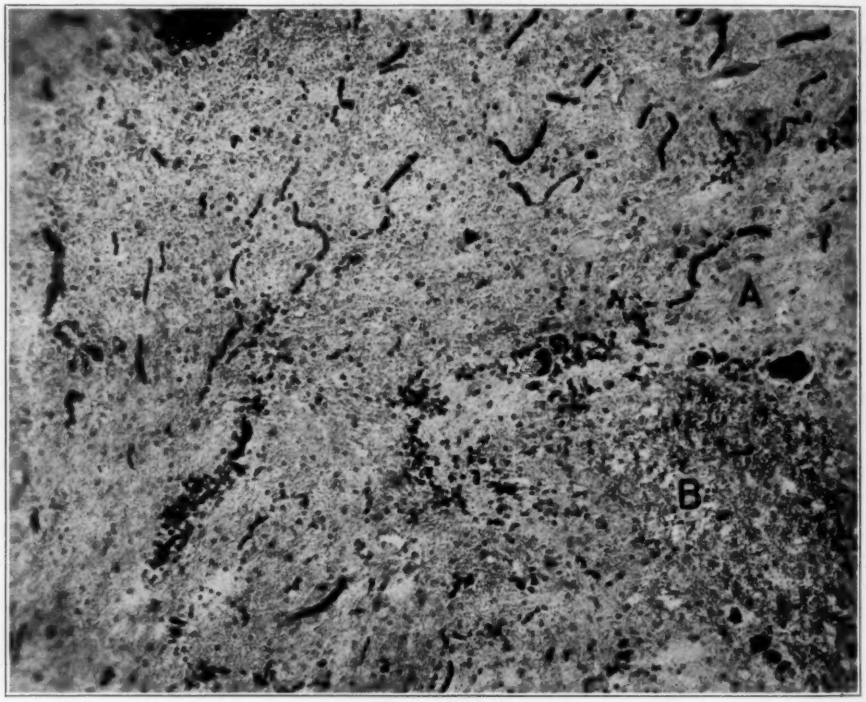

Fig. 8 (case 3).—Section through the lateral horn (*A*) in the upper thoracic level showing congestion and many small hemorrhages more numerous in the gray centers than in the white columns (*B*). Modified Loyez stain.

The pons showed a proliferative and invasive ependymitis, with vascular changes as already described in the periventricular gray, and there was also some congestion in the deeper areas. Myelin stains gave normal results.

Regions about the third ventricle, including the mamillary bodies and the optic tract, chiasma and nerve, the infundibulum of the hypophysis and the medial parts of the thalamus, showed a severe ependymitis, a deep underlying gliosis and vascular changes with proliferation, congestion and hemorrhages. The hemorrhages were especially marked in the gray areas of the thalamus and the mamillary bodies. There was a diffuse gliosis of the optic nerve.

The cerebral and cerebellar cortex showed a diffuse congestion and gliosis, with some areas of organization and tissue softening. The myelin tracts were normal.

Summary and Comment.—There were encephalopathia and myelopathia alcoholica of the hemorrhagic type, with an ependymitis of all ventricles, proliferative and hemorrhagic vascular changes in all of the periventricular gray areas, and congestion and hemorrhage of the adjacent areas of the brain stem and parts of the cerebellar and cerebral cortex. The myelopathy was seen in the proliferative, congestive and hemorrhagic vascular lesions in all parts of the gray areas of the cord and in the marginal softening, which reached its maximum in the mid-dorsal region, where there was something approximating a complete transverse myelomalacia, and there were hemorrhages which passed into the subarachnoid spaces and were seen especially well in the lower levels of the cord. There was a margin of syncytial gliosis, with loss of myelin and fatty changes in the adjacent fibers; also fatty changes in the nerve cells of the cord. Again the lesion was seen to be directly related to the margin of the cord and to the blood supply, being most severe in the lateral horns and the dorsal columns and dorsal roots of the cervical and upper thoracic levels.

The clinical features of importance were an early weakness of the legs with progressive signs in the pyramidal tract, a rapid development of the deep clouding of consciousness with changing rigidities, grasping and groping, and ocular signs, delirious features and profound vegetative disturbances. This case belongs to the first group of alcoholic encephalopathia.

Case 4.—A white woman, married, aged 35, with one living child, was transferred to the psychiatric division of Bellevue Hospital on Feb. 9, 1932, from the City Hospital, with a diagnosis of alcoholic neuritis and cirrhosis of the liver. The City Hospital reported that she had been noisy and destructive, completely disoriented for time and place, and uncooperative, so that adequate physical examination was impossible. The husband gave the history: "One month ago she became sick; the doctor said it was cirrhosis of the liver. Her legs went bad; she had been paralyzed for ten days; she was taken to the City Hospital where she got delirious; she had been drinking heavy for some time." On admission she was disoriented and confabulating; she said, "This is Staten Island. I was drinking here last night. I went home and then went to a lecture. It was by a doctor. I gave birth to the baby this morning. It is a doll. The doctor brought it. My brother brought it."

Examination.—The general condition was poor; the skin was pale, and the pulse rapid. The pupils were unequal; the left was dilated and irregular, but both reacted well to light. There was a leukoma over the right pupil. There was nystagmus in lateral positions. The tongue was reddened and tremulous. The facial muscles were sagging, but showed no paresis. She held her hands in queer postures; the motility was awkward, with athetoid movements of the fingers at rest. There was paresis of both upper extremities, with absent reflexes. There were slight impairment of consecutive touch perception and delayed reaction to pin pricks, with delayed hyperesthesia to more painful stimuli in the upper extremities. The abdominal reflexes were not elicited. There was marked loss of power of the legs, with beginning contractures and bilateral foot drop. The knee and ankle jerks were still present. There was tenderness of the calf muscles and marked hyperesthesia, delayed, to all painful stimuli.

The behavior continued disoriented, confused and tremulous; she was helpless, pulled at the bed clothes, had no control of the arms or legs, had to be spoon fed and was incontinent. She was restless, especially at night, moaning constantly. She misidentified the nurses.

Course.—After February 15, the condition became rapidly worse. There was marked dyspnea, respiration being entirely thoracic in type. There was a delirious type of confusion. The nystagmus was still present and was more marked to the left than to the right. The pupils were small and irregular and reacted poorly to light. At this time there was a right internal strabismus. The athetoid

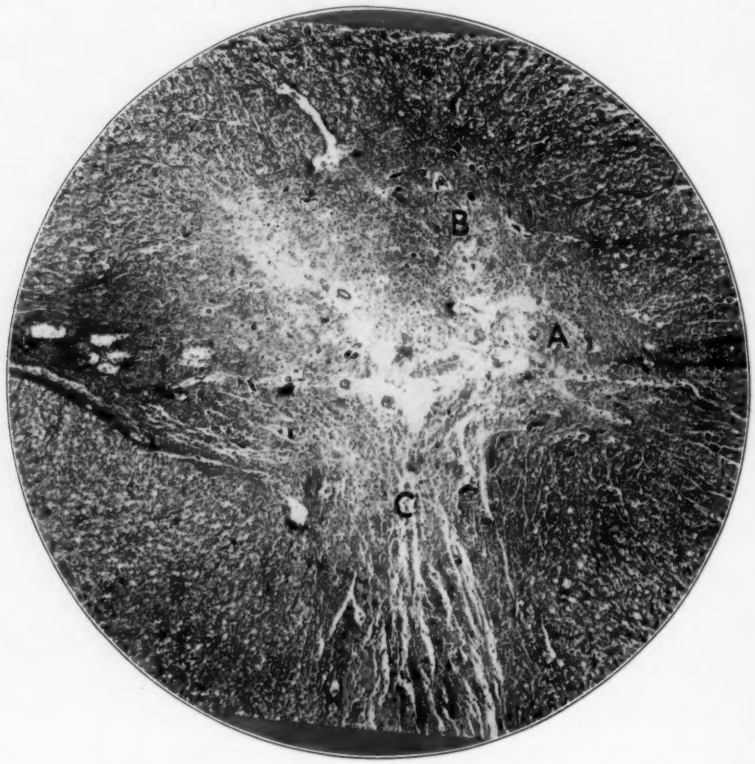

Fig. 9 (case 4).—The midthoracic level of the spinal cord with diffuse congestion, many hemorrhages and softening of the tissue in the center of the gray horn, especially involving the gray vegetative centers about the lateral horn (*A*). There is a slight glial replacement; the cells of the cavity are made up of astrocytes and red blood cells. The anterior horn (*B*) and the posterior horn (*C*) are partially intact. Phosphotungstic-acid hematoxylin stain.

movements of the hands continued. The temperature was elevated to 104 F. The respiratory difficulty become more marked, until a pulmonary edema developed, terminating in death on February 17.

Autopsy.—This was limited to the head and spinal cord. On removal the brain showed considerable pial edema over both parietal lobes, but otherwise neither the brain nor the spinal cord showed any gross abnormalities.

Histopathologic Studies.—In the sacral level of the spinal cord there was some thickening of the pia, with an associated marginal gliosis on the surface of the cord. The nerve trunks showed some swelling of the myelin. The columns and the anterior and posterior horns were intact, but there was some thickening of the anterior central vessels as they passed between the two horns in the lateral position, and some gliosis was observed in this position.

In the thoracic level the same changes were present on the margin of the cord. There was a definite lesion between the anterior and the posterior horn in the gray matter. The nucleus of Clarke, which is present at this level, was normal. In adjacent areas there were small hemorrhages, with softening of the gray matter and a poorly formed gliosis and partial collapse of one side of the cord (fig. 9).

In the cervical level these lesions were more severe. They involved especially the lateral horn, which was sharply contrasted against the normal condition of the adjacent anterior and posterior horns. Glial replacement was very slight.

In the medulla, at the lower end of the fourth ventricle, including the nuclei of the eighth to twelfth nerves, there was a thick wall of ependymitis with an underlying gliosis and vascular changes involving all of the nuclear masses. The lesion was most severe in the lateral recess. There were also epithelial reduplication and vascularization of the choroid plexus. The roots of the vagus nerve showed swelling and fragmentation of the myelin and some increase in the epineurium.

Section through the roof of the fourth ventricle, including the cerebellum with the dentate nucleus, showed the usual changes of the ependyma, with the underlying gliosis and moderate vascular changes, and small hemorrhages in the dentate nucleus. The cerebellar cortex was free from lesions, except for the folia of the lingula which covered the velum, where there was some marginal gliosis.

In the midbrain the reaction of the ependyma and the underlying tissues was of the usual type, typical of alcoholic encephalopathy but of moderate grade. The roots of the fourth nerve showed swelling of the myelin.

A section through the third ventricle, the thalamus and the cerebral peduncles showed severe ependymal changes about the ventricle with a thick wall of gliosis below it. The same lesion covered the surface of the thalamus, but the thalamus itself was relatively free. The massa intermedia was replaced entirely by a heavy wall of glia cells, with numerous small blood vessels and some small hemorrhages. The roots of the third nerve showed moderate myelin swelling.

The optic chiasm showed an increase in fibrous trabeculae and small blood vessels and a diffuse gliosis.

In the cerebral cortex there was a slight marginal gliosis involving the surface of the first layer and a general congestion with occasional small hemorrhages.

Summary and Comment.—There were general reactive ependymitis of all the ventricles, with an underlying reactive gliosis which did not invade deeply; a slight marginal gliosis on the cortical surfaces, the brain stem and spinal cord; slight vascular change with secondary softening in the region of the lateral horn of the spinal cord, and a low grade myelin swelling of the nerves.

The outstanding clinical features were the disturbances in motility and sensibility of the limbs, and the loss of abdominal reflexes. The delayed hyperesthesia was probably a central disorder. There were marked visceral disorders leading to death with respiratory failure. There were athetoid movements, muscular tenderness, loss of tendon reflexes and foot drop. The mental symptoms were characterized by clouding of consciousness and restlessness. Ocular symptoms were conspicuous. This case belongs to the fifth group of encephalopathia alcoholica,

associated with polyneuritis. The pathologic process in the brain showed a moderate marginal gliosis of the cortex and brain stem with the typical ependymal changes associated with an underlying vascular lesion in the ventricular gray areas, including especially the vegetative centers. The same lesion had invaded the spinal cord, especially in the region of the lateral horn nuclei of the thoracic level. Here there were areas of secondary softening associated with hemorrhages. There were some changes in the nerve roots. It was not possible to examine the peripheral nerves.

Case 5.—A Negro, aged 52, was brought to the psychiatric division of Bellevue Hospital on March 7, 1932, by ambulance at the request of his wife, who gave the history that he was a heavy drinker and had not been able to work for several weeks and that for three weeks he had been helpless in bed, unable to care for himself, not realizing what he was doing, and "talking out of his head all the time." The ambulance physician found the patient was shaky, nervous and apparently delirious; he was confused and restless in the ambulance.

Examination.—On admission the patient said, "I have been drinking since Christmas; they took me down here for treatment; they got no room up there; just drinking a little too much; I play the piano. I don't get out on the street and drink whisky. We started it on the fifth of July and kept it up ever since; haven't been eating much lately. I have been blind for three years. I am in Harlem Hospital; I was down here the other day looking for you all." He was restless, helpless, unable to care for any personal needs and showed no interest in them. He was incontinent. Speech was confused, rambling, incoherent and disconnected, and he was disoriented for time and place.

Physically he was emaciated and dehydrated; he had staphylomas of both eyes; the tongue and other mucous membranes were dry and red; there was a tremor of the face and lips with many dissociated movements, with a poor performance of coordinated movements; he was unable to protrude his tongue and an attempt to do so resulted in sucking movements of the lips. There was a generally increased though changeable muscle tonus, though the reflexes were normal. The heart, lungs and abdomen were normal. The spinal fluid was removed under increased pressure, but was clear and all laboratory tests of it, including the Wassermann test, were negative. The Wassermann test of the blood was also negative.

Course.—A week later, in spite of intensive medical and nursing care, the condition had progressed. A severe diarrhea had increased the emaciation and dehydration. The patient was continually excited. He seemed to hallucinate but did not respond definitely to questions. His speech was hardly understandable. He displayed jerky movements in the facial muscles and hands, which were not tremors but irregular quick movements. He made grasping and groping movements and sometimes held his fingers in pointing positions. He also displayed a sucking and grasping reflex. There were changing rigidities in all the limbs, and the irregular quick movements were seen to some extent in the legs, but the abdominal muscles were free. He died on March 19, without showing any improvement.

Autopsy.—This was limited to the head and spinal cord. The meninges were firmly adherent to the brain over both parietal lobes and in these regions appeared thickened and injected. The surface of the brain was definitely edematous. The middle ears appeared normal. The sphenoid sinus contained light green, purulent material. The ethmoid cells appeared normal. The spinal cord showed injection of the vessels in the arachnoid and appeared soft.

Histopathologic Studies.—The sacral level of the spinal cord showed a diffuse vascular lesion, characterized by proliferative changes mostly of the intima of the vessels in both the white and the gray matter. There was also some increase in the perivascular connective tissue, and an increase in the thickness of the pia was seen, with trabeculae of connective tissue invading the spinal cord from the meninges, but there were no actual hemorrhages.

In the midthoracic level of the spinal cord a similar lesion was seen, with an apparent loss of myelin in the dorsal columns and pyramidal and spinocerebellar tracts. This loss, however, may have been only apparent and due to the increase in perivascular and subpial septal connective tissue.

The upper cervical level showed distortion, which was probably due to injury of the soft cord at the time of removal. The diffuse vascular lesion was very severe at this level in both the white and gray areas. The apparent loss of myelin was most evident in the dorsal columns about the blood vessels and marginal to the pia.

In the medulla the lesion was limited to the floor of the fourth ventricle, where it was characterized by a severe proliferative ependymitis of the productive and granular type. There were some proliferative changes of the deeper lying vessels but they were slight.

At the level of the pons a similar lesion was seen about the aqueduct of Sylvius. More severe proliferative vascular changes were seen in the roof, invading the cerebellar peduncles and the lobules of the lingula.

About the third ventricle was a much more severe glial reaction, invasive as well as proliferative.

The cerebral cortex showed some marginal gliosis and some patches of proliferative vascular changes in the subcortical white areas, especially in the occipital lobe. The cerebellar cortex was normal.

Summary and Comment.—Clinically, this case showed many of the characteristic cerebral symptoms of the second group of encephalopathia alcoholica with catatonic features, in the dissociation in the motor and psychic spheres. There were groping, grasping and sucking. The disturbances in the visceral economy were profound and led to death. The pathologic process showed the marginal gliosis, with reactive ependymitis and invading periventricular vascular disturbances. In the spinal cord the lesion was characterized by an increase in perivascular marginal and septal connective tissue. This man was 52 years of age, and these changes may be partly correlated with senile degenerative changes. There was also an apparent diminution in the myelinated fibers, especially of the dorsal columns of the upper levels.

SUMMARY AND CONCLUSIONS

In a previous report by Schilder and myself [1] a series of cases of encephalopathia alcoholica (polioencephalitis haemorrhagica superior of Wernicke) were reported, and several different clinical groups were discussed and correlated with the neuropathologic changes in the brain stem and cortices. It was found that the characteristic lesion was a marginal and ependymal reaction, including a reactive and invasive ependymitis and marginal gliosis with an underlying vascular disturbance, sometimes chronic and sometimes acutely and progressively hemorrhagic. The lesion was related to the proximity to the spinal fluid spaces and the vascular distribution of the related areas. It showed a

specific electivity for the ventricular vegetative gray centers. In one case (case 13) the spinal cord also had a lesion which appeared to be merely an extension of the lesion of the upper brain stem. It showed a marginal gliosis and vascular disturbances invading the gray areas, especially about the vegetative centers in the region of the lateral horn. There was also the case (case 18), in the group with polyneuritic features, of a woman with weakness in the limbs and signs of lesions of the pyramidal tract, spasticity, hyperactive reflexes and a Hoffmann sign, who improved very much and on discharge was free from all these pathologic features.

In this paper, five more cases of encephalopathia alcoholica are discussed clinically, and the histopathologic changes of the brain stem and cortices are reported as before; in addition, studies of the spinal cord were made. The typical lesions of encephalopathia alcoholica were found in all the brains. All of the spinal cords showed definite and similar lesions. In addition to the marginal gliosis related to contact with the spinal fluid, study of the vascular supply of the spinal cord has shown the basis for the vascular distribution of the lesions. For this reason, the lesion has three areas of predilection, differing somewhat in type merely because of the nature of the tissues included in the three areas. The margin of the cord which is affected by its contact with the spinal fluid spaces shows a tendency to thickening of the pia and an increase in marginal and septal connective tissue; in more severe cases there is also a margin of syncytial glial tissue which penetrates into the white columns and is associated with fatty degeneration, fragmentation and loss of myelin in the myelinated fibers. The small peripheral vessels which enter the margin of the cord tend to carry the lesion with them to some extent. The dorsal columns and part of the pyramidal tract, which are supplied by the posterior medial artery which enters the cord through the posterior septum, tend to show a thickening of the perivascular and septal connective tissues which is most severe in the areas nearest to the fissure where the vessels enter. In these areas there is diminution in the myelinated fibers. There are relatively few hemorrhages. But since the same arterial bed supplies the peripheral parts of the dorsal horns there is an associated congestion of this part with numerous small hemorrhages, which especially involve the substantia gelatinosa. The gray horns which are supplied by the anterior medial artery, entering the cord through the anterior fissure as far as the central canal and then fanning out over the gray horns and reaching the areas of Clarke's nuclei and lateral horns first, usually show a severe congestion with more or less numerous small hemorrhages. These lesions are always most severe at the thoracic level of the spinal cord, in agreement with anatomic teachings that this is the part of the cord which receives the most abundant and freshest blood supply direct

from the thoracic aorta. Here the lesions may be so severe that they tend to converge from all these parts and the lesion in the gray areas shows tendencies to break down into areas of softening; gross hemorrhages break through the vessels in the fissures and pass down the subarachnoid spaces to lower levels of the cord. Such lesions may have the pathologic and clinical features of a transverse myelomalacia of the thoracic level. The region of predilection for the most severe lesion is also the part of the cord where are centered the greatest number of nuclear centers of vegetative control, namely, the lateral column horns and Clarke's nuclei of the thoracic level, suggestive correlation between the lesion of the spinal cord involving the vegetative centers of the spinal cord and those about the third and fourth ventricles [1] and the severe disturbance in the vegetative economy of the body as a whole. Disturbances of sensibility are doubtless partly dependent on peripheral neuritis, which was revealed by studies of the peripheral nerve in one of these cases. Nevertheless, the profound lesions in the white tracts of the dorsal columns and other parts, as well as in the gray areas, especially of the posterior horns, also play some part in these symptoms. Signs and symptoms of lesions of the pyramidal tract, such as the Hoffmann and Babinski signs, spasticity and motor weakness, are directly related to the demonstrated lesions in the cord, which sometimes culminate in a severe myelomalacia as well as gross subarachnoid hemorrhages.

In conclusion, in every case of encephalopathia alcoholica in which the spinal cord was studied, a myelopathy was found that appeared to be an extension of the same type of lesion that was found in the upper brain stem and dependent in its distribution on the same factors, namely, the proximity to the spinal fluid about the spinal cord and the distribution of the vascular supply to the spinal cord. The lesion also shows a specific electivity for the vegetative centers, being most severe in and about the lateral horns and Clarke's nuclei and the posterior horns of the thoracic level, but also involving other parts of the cord, especially the dorsal columns and the periphery of these columns.

Dr. Schilder and I [1] showed the correlation between the clinical features in the psychic, motor and vegetative fields of the various clinical groups of encephalopathia alcoholica and the pathologic changes in the cerebral, cerebellar cortices and brain stem. Here there is shown a comparable correlation between the motor, sensory and vegetative disturbances and the lesions in the spinal cords in all cases of encephalopathia alcoholica in which the spinal cord has been examined.

CEREBRAL FAT EMBOLISM

AN EXPERIMENTAL STUDY WITH SPECIAL REFERENCE TO THE REACTION OF THE GLIA

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Fat embolism, which is understood to be the entrance of a liquid oil into the circulation in sufficient quantity to obstruct the passage of blood through the vessels in the various portions of the body, has been little studied experimentally in regard to the effect on the brain. As pointed out by Neubürger, it is found that whereas cerebral air emboli have been studied almost entirely experimentally, on the other hand, the study of the effects of fat emboli on the brain has been confined equally closely to material obtained from autopsies on man. In an extensive review of the literature no reference has been found to an exclusive experimental study of the effect of fat embolism in the tissue of the brain; however, the postmortem studies made by Neubürger and Weimann have given valuable information regarding its cerebral action.

Fat embolism, according to Lehman and Moore, Vance and others, is principally due to injury of the osseous tissue, while other causes of less significance are trauma to the subcutaneous tissues, intramuscular fat and the fatty viscera, burns, intravenous injection of oily substances and poisoning. They further pointed out that fat embolism has been found in cases of diabetes, eclampsia, acidosis, carbon monoxide poisoning, profound sepsis, chronic alcoholism, chloroform narcosis, diabetic retinitis, phlegmonous gastritis, acute pancreatitis, chronic tuberculosis, menstrual suppression, hepatitis, splenitis, carcinomatosis and sarcomatosis. Landois found most cases of fat embolism to occur in persons between the ages of 20 and 50 years. Gauss explained why trauma is the leading cause, as the following logical requirements are fulfilled: first, injury of the adipose tissue with the liberation of free fat; second, rupture of vessels, especially veins, in the abraded area; third, establishment of a mechanism whereby free fat passes into the open ends of blood vessels. The third requirement is met in the osseous tissue more readily than in the other tissues of the body, for the bony canals

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aid in holding open the ends of the lacerated vessels, allowing the negative pressure in the venous system to aspirate the liberated fat.

When free fat is liberated in the blood stream it is first carried to the lungs, giving rise, as Payr (quoted by Vance) pointed out, to pulmonary embolism, and later the fat arrested here may be pressed through the capillaries of the lungs into the general circulation, going to other organs of the body, especially the brain, and giving rise to what has been termed cerebral fat emboli. The emboli in the lungs and in the brain in turn cause, according to Gröndahl, two distinct clinical pictures. The former, the pulmonary type, has an onset of symptoms soon after injury, with marked cyanosis and edema of the lungs and early death in fatal cases. The latter, the cerebral type, allows a feeling of well-being for several hours or even several days after the injury; this is followed by restlessness or even delirium and finally coma preceding death.

Gröndahl estimated that 46 per cent of the deaths in cases of fat emboli are due to the cerebral type. He considers the brain as one of the most potent filters for fat and attributes the frequent injury of the brain, even in cases in which the lungs are not affected sufficiently to produce symptoms, to fat emboli in this region. He based his conclusions on the following facts: First, the brain is comparatively rich in blood supply. He has shown by comparative figures that given a brain weighing 1,200 Gm. and kidneys, 300 Gm., the brain gets 1,632 cc. of blood in a given time while the kidneys get only 300 cc., demonstrating that the largest amount of the homogeneously fat-saturated blood would go to the brain. Second, the vessels of the brain are narrow. He found that the capillaries of the brain are even smaller than those in any other organ. Next he found that the size of the fat droplets varied little when free in the blood stream, thus proving the filtration power of the brain. Finally, he showed the great vulnerability of this organ, stating that the brain suffers severely when fat passes from the pulmonary to the cerebral circulation, and that the reason there are not more deaths due to cerebral conditions is that parts of the brain can substitute for each other so that clinical symptoms arise only from large lesions. Weimann agreed with Gröndahl and considered further that the destruction in the brain in many cases is sufficient to explain the cause of death. On the other hand, Paul and Windholz considered that the areas are of minor importance.

From the pathologic standpoint, the best descriptions in the literature are case reports by Weimann and Neubürger. They found that in their cases the brain was everywhere involved. Neubürger concluded that the intensity of the pathologic process varied directly with the profuseness of the capillary bed of the part involved. The dentate nucleus was most affected, while the intensity subsided in the following localities in

the order named: olive, striatum, cornu ammonis, cortex and white matter. The usual pathologic picture in the brain, as described by Spielmeyer, such as hemorrhagic areas, necrosis, edema and fat in the capillaries, was noted by these authors as well as by all who have made similar studies.

In this article a study was made of the pathologic changes in the brain caused by fat embolism, with especial reference to the reaction of the glia. The lesions caused were followed grossly and microscopically

Experimental Procedures

Rabbit	Time Allowed to Live After Operation	Procedure
1	.....	Nonoperative control
2	5 days	Operative control
3	3 days	Operative control
4	.....	Nonoperative control
5	2 hours	Injection of 8 minims of stained oil
6	2½ hours	Injection of 8 minims of stained oil
7	3 hours	Injection of 8 minims of stained oil
8	4 hours	Injection of 8 minims of stained oil
9	8 hours	Injection of 8 minims of stained oil
10	12 hours	Injection of 8 minims of stained oil
11	24 hours	Injection of 8 minims of stained oil
12	48 hours	Injection of 8 minims of stained oil
13	52 hours	Injection of 8 minims of stained oil
14	3 days	Injection of 8 minims of stained oil
15	4 days	Injection of 8 minims of stained oil
16	5 days	Autogenous injection of 8 minims of oil
17	5 days	Operative control
18	5½ days	Injection of 8 minims of stained oil
19	6 days	Injection of 8 minims of stained oil
20	7 days	Autogenous injection of 8 minims of oil
21	7 days	Injection of 8 minims of stained oil
22	10 days	Injection of 8 minims of stained oil
23	14 days	Injection of 8 minims of stained oil
24	19 days	Injection of 8 minims of stained oil
25	22 days	Injection of 8 minims of stained oil
26	24 days	Injection of 8 minims of stained oil
27	26 days	Injection of 8 minims of stained oil
28	30 days	Injection of 8 minims of stained oil

from their inception until thirty days had elapsed. This was undertaken in view of the fact that the literature gave no data regarding the chronologic development of the pathologic changes in this condition.

TECHNIC

The technic chosen was such as to give absolute control of the factor of time in order to correlate the changes which take place in the brain following fat embolism. This was done by injecting the oil directly into the common carotid artery, giving a condition that is impossible, clinically, yet serves best in showing chronologically the pathologic condition induced in the brain after the fat has passed through the capillaries of the lungs. The experimental animals used were grown rabbits, because the microglia is more easily stained in rabbits than in other animals. Preference for grown animals was due to the size of the carotid, a mechanical consideration.

Eight minims of olive oil which had been previously stained to its maximum with scarlet red, filtered and sterilized was injected into the carotid artery of each rabbit, except the controls (table). The operation was done under regular operative aseptic technic. The controls consisted of two animals which had not been operated on, two which had been given injections of oil obtained from their perirenal adipose tissues and three in which a craniotomy was performed and a unilateral aseptic injury of the brain was produced by cutting or puncture. The controls, receiving an injection of oil obtained from the perirenal fat, were operated on in the morning and the fat removed by means of an abdominal incision. The fat was heated just sufficiently to liberate the oil, after which the oil was placed immediately in a refrigerator and, in the afternoon of the same day, was sterilized in an autoclave and then injected into the carotid artery just as in the case of the stained oil. Care was taken that each of these rabbits was given an injection of the oil obtained from his own fat.

Ether anesthesia was used in all cases. The vessels were handled as gently as possible, and no ligatures were used on the vessels into which the injections were made. Bleeding following the withdrawal of the needle was stopped by bringing the muscle in contact with the opening in the vessel. The incision was closed in the usual manner.

Following this procedure the rabbits were allowed to live for a given interval, varying from two hours to thirty days, and then killed. Death was brought about in the controls and experimental animals alike; ether was administered, the carotid artery was exposed and a fixing solution of formaldehyde ammonium bromide was injected into the artery until death occurred. Following death the brain was immediately removed, cut in sections from 4 to 5 mm. in thickness, and placed in formaldehyde ammonium bromide for three days, at the end of which time some or all of the following slide preparations were made: (1) Lorraine Smith stain; (2) scarlet red stain; (3) silver carbonate stain for microglia; (4) gold sublimate stain for astrocytes; (5) combined silver carbonate stain for microglia and scaret red; (6) gold sublimate stain for astrocytes combined with scarlet red; (7) hematoxylin and eosin stain.

EXPERIMENTAL OBSERVATIONS

All of the brains were examined macroscopically; briefly, the following results were obtained: The brains of rabbits 2, 3 and 17 had a small scar to which the meninges were attached; the edges of the scar were slightly raised above the surrounding tissue. The other rabbits showing any abnormal changes were rabbits 5, 6, 7, 8, 9, 10 and 11. The brains of these animals were somewhat enlarged and edematous, especially on the side on which the injection was made. The coloration from the stained oil could be seen to extend across the midline about 2 mm. into the opposite cerebral hemisphere. No hemorrhage was seen, but this could easily have been invisible, owing to the stained oil used in the experiment. These were the most important of the macroscopic findings. The article will be confined from now on almost entirely to a microscopic study.

Before proceeding, however, it seems appropriate to mention briefly the clinical symptoms observed. Opisthotonos developed in several animals immediately following the operation; none of these survived over a few hours; they were not used in the experiment. Only two of the animals which survived showed any clinical manifestations. Rabbit 8 showed loss of interest, fear and appetite. Rabbit 15 showed paralysis of the right front leg and of the muscles of the right eye and cerebellar symptoms.

Controls.—The more significant results found microscopically follow:

Rabbits 1 and 4 were nonoperative controls. No pathologic condition was found in the brains by any of the stains used. Occasionally a monocyte, the clasmatocyte of Kubie, which contained fat as shown by the scarlet red stain, was found lying along the adventitial sheath of a vessel.

Rabbits 2, 3 and 17 were operative controls. In each of these one side of the brain was injured and the other side left intact. In the injured side the changes were exactly as described in rabbits 1 and 4. In the injured area there was the typical reaction to trauma of the parenchyma of the brain as has been described by Hortega, Penfield and others. By superimposing scarlet red on the silver

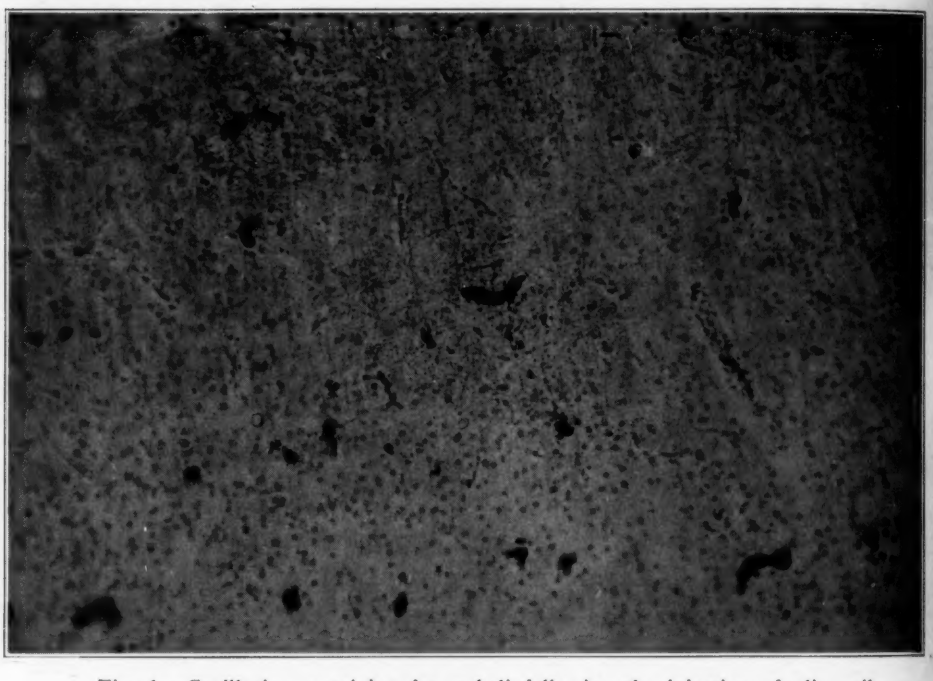

Fig. 1.—Capillaries containing fat emboli following the injection of olive oil into the carotid artery. Scarlet red stain.

carbonate stain, it was noted that these enlarged microglia cells, particularly the gitter cells, were loaded with fat. Many of the transitional cells also contained much fat. Some of the cells containing fat were near capillaries, quite distant from the edge of the lesion. The gold sublimate reaction, resembling that described by Penfield, showed a large increase in the size of the astrocytes around the injury, with their processes somewhat radially arranged toward the lesion. There was proliferation of the connective tissue in and around the area of injury.

Experimental Animals.—Rabbit 5 was allowed to live for two hours after the injection of stained oil. The Lorraine Smith stain showed large amounts of neutral fat in the capillaries. Other stains used gave no further evidence of pathologic change (fig. 1). However, it should be stressed that Nissl, axon or

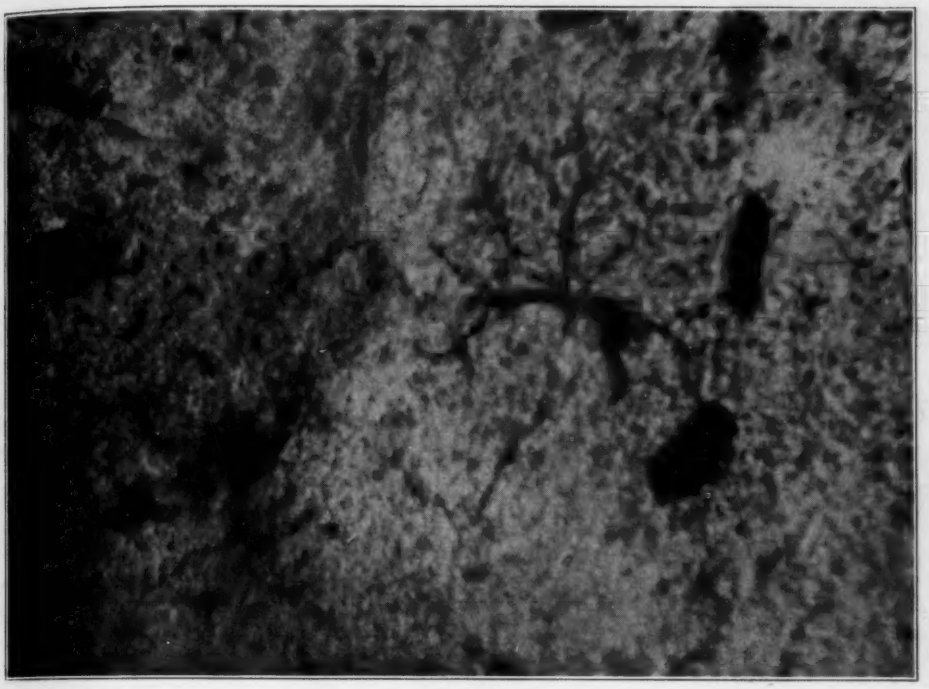

Fig. 2.—Microglia containing fat in the cytoplasm of the cell body near the nucleus. Scarlet red superimposed on the silver carbonate stain.

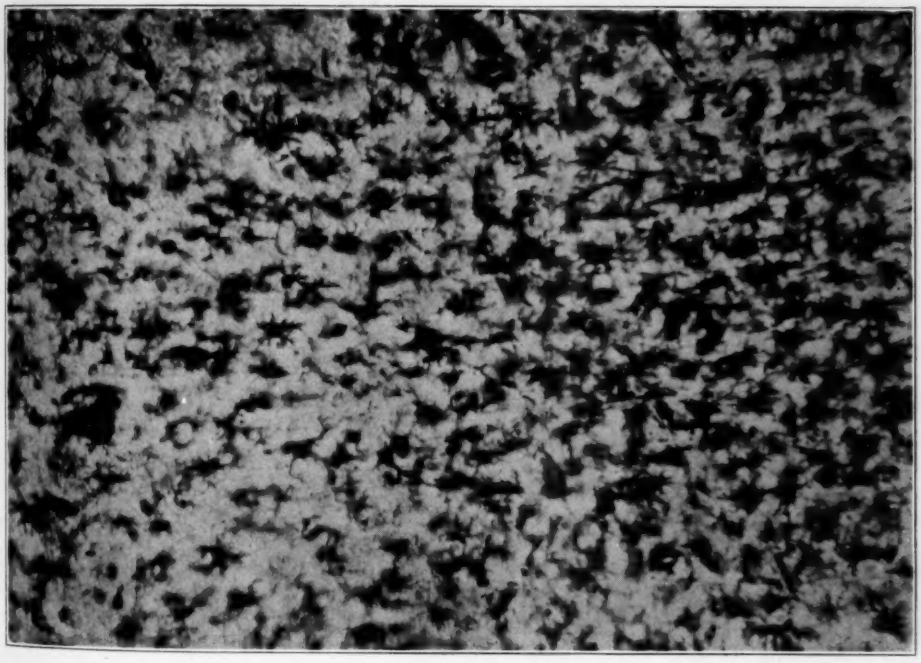

Fig. 3.—Reaction of the microglia to vascular disturbance showing transitional and some gitter cells. Silver carbonate stain.

myelin sheath stains were not used, since the interest in this paper is focused on the glia rather than on the nerve cells and axons.

Rabbit 6 was allowed to live for two and one-half hours after the oil was introduced into the carotid. There was a rather large fresh hemorrhage, and numerous petechial hemorrhages were noted around capillaries. Numerous capillaries were filled with neutral fat, but there was no glial reaction to either the hemorrhage or the emboli.

Rabbit 7 was allowed to live for three hours after injection. Similar results were obtained as with the animals already described, except that there were no hemorrhages.

Rabbit 8 was permitted to live for four hours after injection. Neutral fat continued to fill the capillaries. At this time some of the microglia contained small amounts of fat, as shown by the combined microglia and scarlet red stain. The microglia showed little change in either size or form, and one could see, unmistakably, small amounts of fat lying in the cytoplasm closely associated with the nucleus. No other type of cell showed fat within its cytoplasm (fig. 2). The cells containing fat seemed to have no particular relationship to the capillaries containing fat emboli. The other types of cells appeared to be intact; at least they were not undergoing fatty change.

Rabbit 9 was allowed to live for eight hours after injection. On microscopic examination it was seen that part of the fat in the capillaries stained red and part violet, the red being neutral fat and the violet portion fat which had undergone some change. More microglia containing fat could be demonstrated at this time than at the four-hour stage.

Rabbit 10 was killed twelve hours after injection. Numerous capillaries contained neutral and changed fat. Many microglia cells contained fat, without any great material change in their form.

Rabbit 11 was allowed to live for twenty-four hours after injection. There still remained neutral fat in some of the capillaries, but most of the emboli had undergone change as shown by the Lorraine Smith stain. The microglia contained fat. The only other pathologic change seen in the sections of this rabbit was petechial hemorrhages around some of the capillaries. The superimposed scarlet red on the gold sublimate stain showed some capillaries containing fat stained a brilliant red, and around this a small circle in which the extravasated blood gave a deep green color with gold sublimate.

Rabbit 12 was killed forty-eight hours after injection. Practically all of the fat had disappeared from the capillaries, only a few containing fat emboli. Fat continued to be present in the microglia.

Rabbit 13 was allowed to live for fifty-two hours after injection. Practically all of the fat had disappeared from the vessels, yet there was still fat in the microglia. No fat emboli were seen. The brain of this rabbit showed many petechial hemorrhages scattered throughout and in one small area a beginning proliferation and swelling of the microglial derivatives around a region of petechial hemorrhage.

Rabbit 14 was killed three days after injection. Fat continued to be present in the microglia. Only a small amount of fat was present in the vessels.

Rabbit 15 was killed four days after injection. There were found petechial hemorrhages, as has been described previously. No fat was found in the vessels or in the microglia.

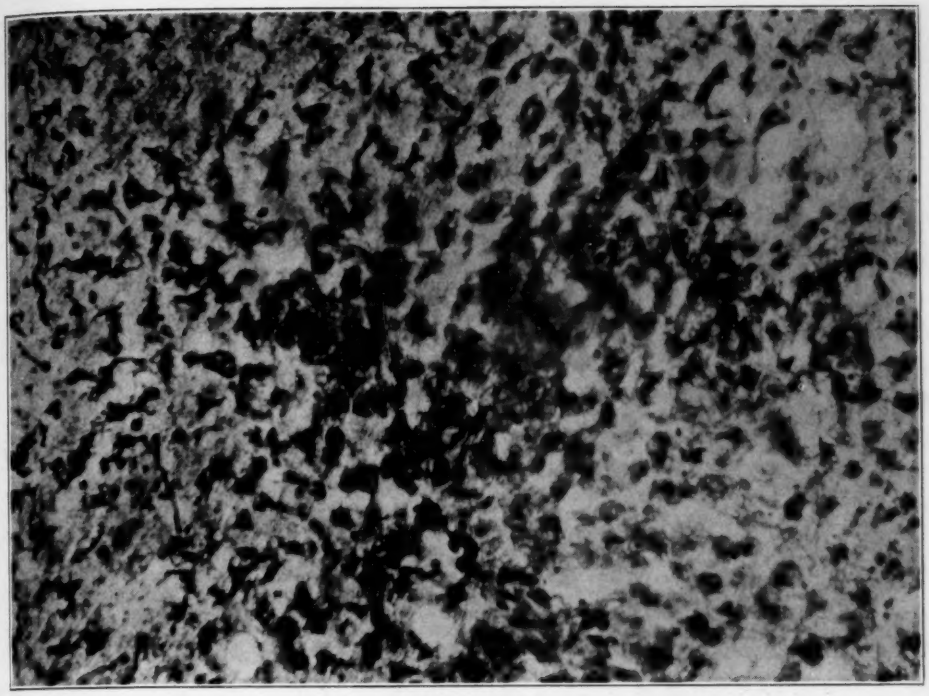

Fig. 4.—Circular area of gitter cell reaction due to the destruction of the parenchyma of the brain following embolism. Silver carbonate stain.

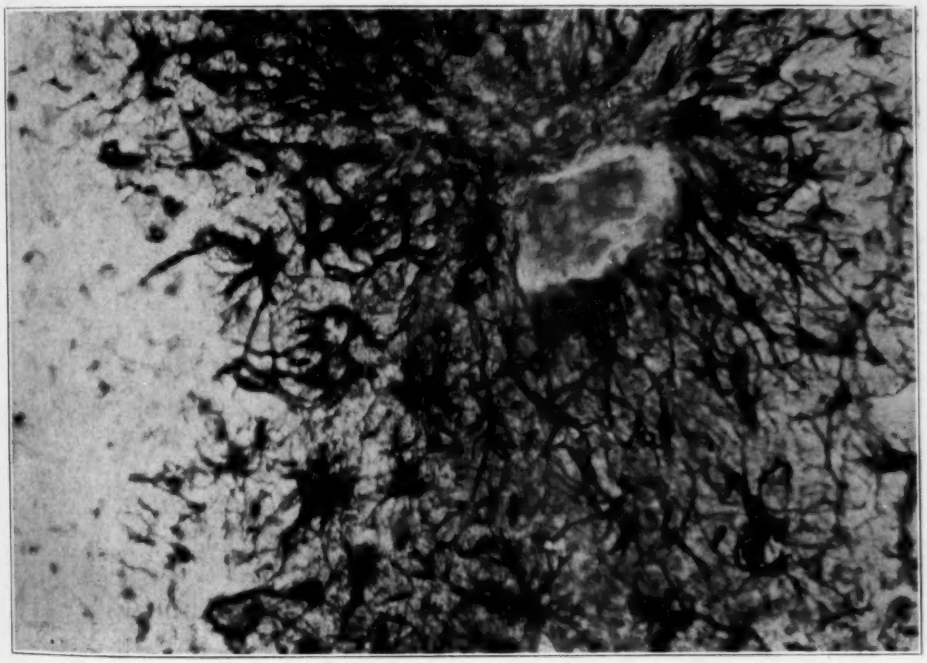

Fig. 5.—A region showing astrocyte reaction on the right to an area of necrosis on the left. Gold sublimate stain.

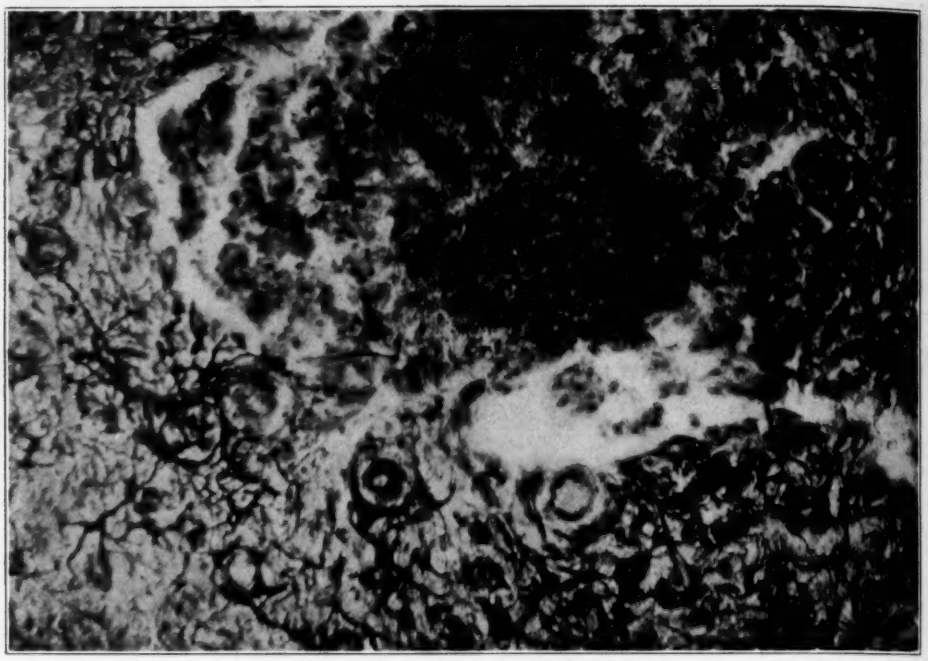

Fig. 6.—An area of central necrosis surrounded by gitter cells. This is surrounded by a zone of enlarged astrocytes. Gold sublimate stain.

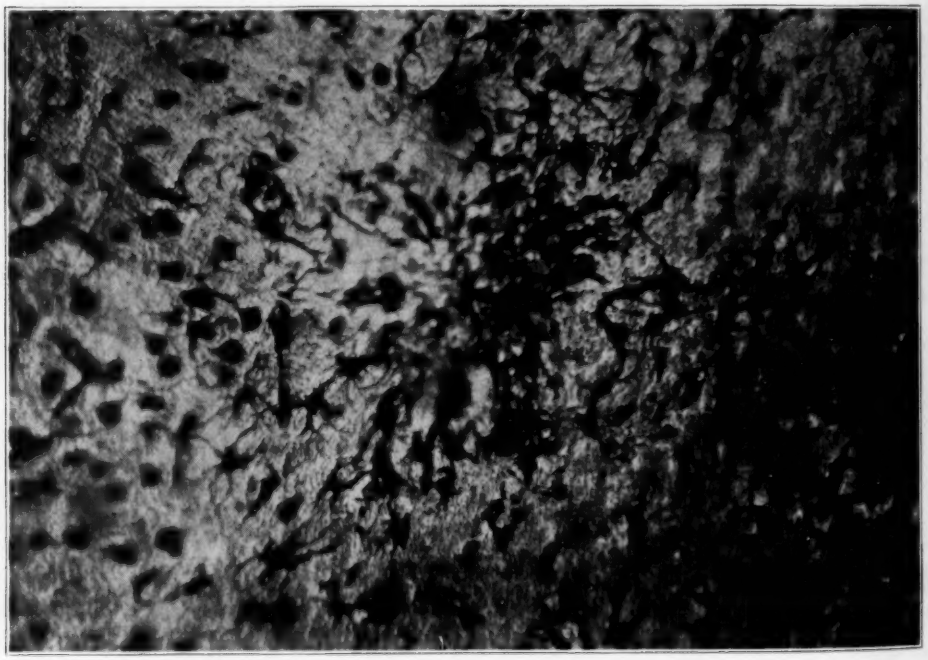

Fig. 7.—An area of healing in the parenchyma of the brain showing astrocytes increased in size and number with their processes radiating toward the center. Gold sublimate stain.

Rabbit 16 was allowed to live for five days after injection. This animal was given an injection of oil rendered from its own perirenal fat so that we might note the difference between the reactions of the brain to stained olive oil and autogenous fat.

On microscopic examination, the silver carbonate stain showed large regions in which there was a marked glia cell reaction, all of the cells here appearing to be in the later stages of transition rather than definite gitter cells (fig. 3). These localized lesions were ill defined and faded off into areas in which the microglia appeared more nearly normal. There were still other regions in which definite necrosis was found, with the compound granular corpuscles near the necrotic focus and the transitional cells a little more peripheral and gradually fading off into more nearly normal microglia (fig. 4). The gold sublimate stain showed several large regions which were degenerating. These were pale, with no definitely distinguishable cells of any type. The degenerating region was surrounded by enlarged astrocytes which, as a rule, sent their processes toward the necrotic region; the cells appeared increased to about five times their normal size (fig. 5).

Rabbit 18 was killed five and one-half days after injection. The changes in this animal were similar to those in rabbit 16.

Rabbit 19 was allowed to live for six days after injection. There were found in this animal regions of necrosis with astrocyte and gitter cell reaction as described in rabbit 16.

Rabbit 20 was killed seven days after injection. No areas of softening were encountered.

Rabbit 21 was killed seven days after injection. This was another animal into which oil extracted from its own fat was injected; in it zones of softening, with gitter cell and astrocytic reaction, as described in the other animal, occurred.

Rabbit 22 was killed ten days after injection and nothing pathologic was found.

Rabbit 23 was killed fourteen days after injection. A zone of rarefaction, with astrocytic reaction around it, as previously described, was encountered in the sections stained with gold sublimate. This condition was not seen in the sections stained with silver carbonate. There was a large amount of free fat in the capillaries, and more than the normal amount of fat was seen in the cells around the vessels, which appeared otherwise normal. The Lorraine Smith stain showed that this was not neutral fat.

Rabbit 24 was allowed to live nineteen days after injection. The slight changes found in the stained sections could not be considered a result of fat injected.

Rabbit 25 was killed twenty-two days after injection. An area in the section stained with gold sublimate showed a region of central necrosis surrounded by cells resembling gitter cells, and this was encircled by astrocytes which were very much enlarged in size and increased in number. Among these astrocytes was a proliferation of connective tissue from the vessels in the region (fig. 6).

Rabbit 26 was killed twenty-four days after injection. No areas of necrosis were found.

Rabbit 28 was allowed to live thirty days after injection. The sections stained by the gold and silver methods were found on macroscopic examination to show a V-shaped region of degeneration, the vertex of the V pointing interiorly toward the white matter. The gold sublimate stain showed enlarged astrocytes, with their processes directed toward the lesion, where they intermingled with the connective tissue dipping down from the meninges and proliferating from the vessels in the vicinity. Among the astrocytes were masses of gitter cells, which became more numerous as one approached the edge of the lesion. Numerous capillaries contained much fat which had been deposited by the gitter cells.

COMMENT

In this experiment it was possible to follow some of the changes which take place in the glia of the brain in cases of fat embolism. These changes will be discussed, so far as possible, in chronologic order.

The immediate result of the liberation of fat into the common carotid artery was the formation of cylindric and spherical fat emboli in the capillaries of the brain (fig. 1). Of course, not all the fat went to the brain, some going into the other branches of the common carotid and forming emboli in other tissues. The fat which went into the cerebral circulation was generally distributed over the entire hemisphere supplied by the artery, as shown by Neubürger, Gröndahl and Weimann, more going to the areas of greatest capillary supply, as previously mentioned.

It has been the general opinion of those who have used the method of injecting fat into the common carotid—Wiener (quoted by Fuchsig), Fuchsig, Reuter and Scriba—that in case the fat did not cause early death by sudden ischemia of the brain it would pass on without producing any great amount of injury and practically all be filtered out of the general circulation by the lungs. It is true, in view of the fact that they have found much fat in the lungs soon after intracarotid injection, that much of the fat passes on through the capillaries of the brain and goes to other organs, but a significant amount remains to be removed only by physiologic methods other than the circulation and by pathologic processes. Gauss stated that the possible ultimate disposal of free fat from the general circulation may be accomplished by the following means: First, it lodges in the glomeruli of the kidneys, whence, by capillary rupture or intercellular openings, it passes into the urine; second, some may be excreted in the bile into the intestine; third, some may be digested by phagocytic cells; fourth, some may be emulsified by the mechanical action of the blood current aided by the saponifying action of the blood lipase and be reabsorbed into the tissues. It would appear that the brain participates as a significant factor in removal of fat by the last two methods.

In regard to the idea that fat passes through the cerebral circulation, Gröndahl showed, as pointed out earlier in this paper, that the brain is a potent filter. It seems, in a review of the literature, that all the capillaries of the body play an important rôle, for, as has been shown by Vance, petechial hemorrhages in the skin are a diagnostic criterion, and fat emboli have been reported in practically all organs. This being true, the extent of embolism resolves itself into a question of blood supply and position of the organ in relation to the fat-laden blood. Because of the strategic anatomic position of the lungs in relation to organs from which fat emboli may be liberated, it is natural that they

should receive most of the burden. However, practically every authority agrees that the filtration by the lungs is not perfect and that the emboli do get through into the general circulation. This fact puts the filtration power of the lung or any organ, then, on a basis of the amount of its circulation and its position. Since the lungs occupy the position they do, one would say that on them lies the greatest burden, but after the emboli escape from the capillaries of the lungs the brain becomes the next greatest filter for, as has been shown by Gröndahl, its supply of blood is much greater than that of any other organ.

By means of the injection of stained fat, it was brought out, as has already been shown by Cobb, that there is an overlapping of the circulation of one side of the brain with that of the other, indicating further a capillary anastomosis and an absence of the true end-arteries in the brain. In this experiment it was found that on injection of the stained oil into the right common carotid the whole right hemisphere was diffusely stained, and this stain extended approximately 2 mm. from the midline into the left cerebral hemisphere. Such a line of demarcation could not be accounted for by the oil passing to the left side via the circle of Willis.

There was considerable edema of the side of the brain supplied by the carotid artery into which oil was injected. A noteworthy observation was the small number of petechial hemorrhages seen. Macroscopically, of course, they could not be seen at all because of the stained fat content, and on microscopic examination they were found in only a few cases. This observation is at variance with the expected results, for the opposite was noted in all the literature read. One might consider that the reason for this result lies in the fact that only a small amount of fat was injected and that in clinical cases or experimental cases of injection into veins the fat is liberated from the lung capillaries in showers, an amount exceeding the 8 minims injected in this experiment. But even in similar intracarotid injections in which a smaller amount of fat was injected, as shown by Daddi, there were reported multiple petechial hemorrhages.

How these hemorrhages are caused is a question for discussion. Most investigators consider them to be minute infarcts; Gröndahl said that they are due to blood extravasated from the vessels around an area of infarction, but Weimann considered it impossible to determine the mechanism of their origin. In this experiment the only hemorrhages seen were very small, circular areas surrounding a vessel, and, in most cases, the vessel could be shown to be closed with fat, except in the case of one larger and more diffuse hemorrhage. No circular zones of hemorrhage were demonstrated around necrotic areas.

It was found, as reported by Landois, Gröndahl and others, that more of the emboli lodge in the gray matter and that there is more

hemorrhage in the white. It was also found that the number of regions of destruction were greater in the white matter, but the size of the destroyed areas was larger in the gray. Since the theory of end-arteries in the brain, as upheld by Spielmeyer and others, has been overthrown by Cobb, this finding remains well explained by Weimann, who stated that where the capillary supply is best, there are more emboli and less necrosis. This is known as the *Gefässfaktor* of Spielmeyer. The fact that there were larger lesions in the cortex than in the white matter is easily explained in that the arteries of the cortex are larger than the capillaries of the white matter, and whereas the capillary supply of the cortex is sufficient to prevent a destructive phenomenon when only a capillary is involved, there is not sufficient anastomotic circulation to compensate for a larger vessel.

Should Gröndahl's idea be considered correct, that the size of the fat drops varies but little, the explanation becomes more difficult unless one considers that a thrombosis extends from the lodged fat embolus toward the periphery of the cortex. It seems more logical to assume that there is a variation in the size of the fat droplets and that they lodge temporarily in vessels according to their size, the larger vessels impeding the larger fat droplets. It may be further assumed that the temporary stoppage causes a local ischemia, initiating a progressive destruction of the area of parenchyma supplied by the vessel although the fat passes on. In contradiction to the finding of Daddi that fat is always deposited in small droplets in the capillary, in this experiment numerous long cylinders of fat were found, and it would appear that, to begin with, these cylinders were rather large drops of fat, for had they been small droplets, there would have been an appearance of beading rather than a compact cylinder. Too, there were seen large drops of fat entirely filling the lumens of the small precapillary vessels which were quite capable of causing a large area of destruction.

Weimann and Fuchsig considered the capillaries as permeable for the fat. In this experiment it was found that, four hours after injection into the carotid, fat could be demonstrated in the microglia, an observation confirmed by the recent work of Daddi. Here it was found that fat could be detected in the microglia from four to seventy-two hours following injection. It was considered possible that such a demonstration would be possible for even a longer length of time for, as shown by the Lorraine Smith stain, the injected fat does not disappear entirely for about four days following injection. Daddi showed in his experiment that all of the injected fat had disappeared from the capillaries within twenty-four hours, but since he injected smaller amounts it is possible that the rapidity of disposal depends, to some extent, on the amount injected.

As shown in this experiment and also by Daddi, the microglia take up the fat without any marked change in size or shape. The fact that the fat was demonstrated only in the microglia and that no other cells showed any sign of fatty degeneration makes one consider that the fat seen in the microglia was fat consumed, which had passed through the capillaries, rather than fatty degeneration of the cell itself. This finding is in confirmation of the work of Hortega and Penfield, which showed that the microglia are the phagocytes of the brain.

Not until five days had elapsed following the injection did one see a true microglia reaction, with the formation of gitter cells. This finding is comparable to that which Spielmeyer observed in his work with air embolism. From five days on, regions of gitter cell reaction showing degeneration of the parenchyma of the brain were found in the cases in which lesions were encountered.

To prove that the damage to the parenchyma of the brain was due to the emboli as such, rather than to toxic reaction to the foreign oil or the stain used in the oil, two rabbits were given injections of unstained oil rendered from their own fat, and in both cases there was found extensive pathologic change in the parenchyma of the brain, which was similar in every way to the lesions from the injections of the stained olive oil.

In substantiation of the finding of Penfield, in which he described the microglial derivatives phagocytosing the material of brain destruction in cases of glioma and transporting it to the vessels into which it was deposited, it was found in this experiment that following the appearance of gitter cell reaction the capillaries are again loaded with fat, as demonstrated by the scarlet red stain superimposed on the silver carbonate. The vessels containing this fat are almost as numerous around the areas of reaction of the parenchyma of the brain as those just after the injection of the fat into the carotid. Ameboid gitter cells containing stained fat are seen lying close to and in contact with the capillaries, even fairly distant from the region of necrosis.

Around the necrotic lesions the astrocytes acted in accordance with the results obtained by Hortega and Penfield in their experiments on stab wounds. There was an increase in the number and size of these cells, and they were radially arranged with their processes extending in the direction of the necrotic area. Healing was brought about in the areas located in the parenchyma of the brain by a gliosis. The astrocytes arranged themselves radially around an area of connective tissue which had proliferated from neighboring vessels, as described by Hortega and Penfield. In the larger areas at the periphery of the cortex, the connective tissue was seen to dip down from the meninges, and the processes of the astrocytes interlaced with the connective tissue as shown previously by Penfield.

SUMMARY AND CONCLUSIONS

In this series of experiments, twenty-eight rabbits were used, seven of them as controls. Two of the seven controls received injections of oil obtained from their own perirenal fat and these showed as much pathologic change as any of the twenty-one test animals which received injections of olive oil stained with scarlet red. The controls that received parenchymal damage to the brain showed the typical gitter cell reaction around the area of trauma.

Macroscopically, there was edema, principally on the side on which the injection was made, for about fifty hours following injection. One could see from the disposition of the stained oil that the smaller vessels of both sides of the brain intermingled for about 4 mm. in the midline. No hemorrhage was seen on gross observation as the result of the injection of the stained oil, and in view of the reports in the literature it was both surprising and interesting to find so little hemorrhage even microscopically.

By using scarlet red superimposed on silver carbonate, fat was demonstrated in the microglia as early as four hours, and as late as seventy-two hours after injection. This appeared to be phagocytosed fat which escaped through the physiologic openings in the capillaries. No fat was present in any other type of cell.

The fat injected was found to have undergone chemical change within two days after injection, and no trace of emboli of either neutral or chemically altered fat could be demonstrated after four days. It was not until five days had elapsed that definite areas of destruction in the brain with transitional and gitter cell reaction were demonstrable.

In healing, the small lesions in the parenchyma of the brain showed a proliferation of enlarged astrocytes whose processes radiated toward the center of the region which often contained a small amount of connective tissue emanating from the small vessels close by. Larger lesions in contact with the meninges showed connective tissue proliferating from the meninges and vessels of the brain in the vicinity of injury, interlacing with the processes of the enlarged astrocytes which radiated to the border of the destroyed region.

Finally, from this experiment it can be concluded that when free fat reaches the brain by means of the blood vessels the following may occur: (1) The fat may pass through without causing any appreciable damage; (2) it may result in embolism. When the latter occurs, after two and one-half hours petechial hemorrhages are found; after four hours a portion of the fat has passed through the vessel wall and is taken up by the microglia. Five days following embolism necrosis takes place, with the usual reactions of the microglia, astrocytes and connective tissue.

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DREAM ANALYSIS

ITS APPLICATION IN THERAPY AND RESEARCH IN MENTAL DISEASES

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Accumulated evidence supporting the value of dream analysis as an aid in the understanding and treatment of mental disease has now reached a stage at which it is hardly possible for even the most skeptical to doubt its usefulness as a method in clinical psychiatry. Regardless of how far one wishes to go in accepting all the claims made by some extreme proponents, it must be admitted that the neuropsychiatrist can get a great deal of help in clinical work from a thorough study of the dreams of patients. In a recent contribution on this subject Kretschmer [1] summed up aptly the present status of the problem in the statement: "It is not a question now as to whether we are justified in using the dreams of our patients in passing judgment on their condition, but rather a question whether we are justified in *not* doing so." It must be emphasized, however, that most of the reported material deals with the proof of the validity of dream analysis as an empirically established clinical method, although in the progress of its development, dream psychology, at least in its theoretical aspects, has reached out for broader implications. Thus, the psychoanalytic school, which was responsible for the introduction of dream analysis, and workers in allied fields have not been entirely satisfied with the use of dream analysis in a purely therapeutic capacity and have extended it into the realms of theoretical psychology and psychopathology. With these attempts a new problem has been introduced, which is concerned not so much with the practical use of dreams in clinical psychiatry, as with their use in the establishment of theories concerning human behavior and the laws that govern it. The question to be considered is, therefore, whether the material thus far obtained is valid as a basis for studies of this type.

The problem is of interest not only to the theoretical psychopathologist; it is the concern of the clinician as well. Methods established purely empirically may be useful, and the field of medicine in general

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1. Kretschmer, E.: Das Ressentiment im Traum, Arch. f. Psychiat. **96**:227, 1932.

has derived a great deal of benefit from them. To be reliable, however, a method must always aim for rational support in terms of experimental proof. It is only on such a basis that the effect of the method can become predictable in terms of certainty or, at least, probability, instead of being left in the rather foggy realms of possibility. It is essentially from this point of view that Kretschmer, in the article quoted, while realizing the value of the work done so far, expressed the opinion that the time has come for ". . . earnest investigation . . . of dream material not in terms of fantastic interpretations, but through accepted experimental methods such as ascertaining the frequency of coincidence of two types of experiences, etc."

Since its inception, however, the field of dream psychology has spread and grown to large proportions until it has reached a point where it includes as large a variety of subjects as experience itself. To be systematic, investigations in this field will have to deal with isolated concepts that have been advanced rather than an attempt to study the field as a whole. It was with this in mind that in a previous article [2] on this subject I suggested that for practical purposes it would be best to undertake a series of experimental investigations dealing with the different aspects of the problem in a systematic way. Unless one can prove that the knowledge previously gained is not only true of a given person but can be experimentally reproduced in such a way that it is shown to be true of the group as well, the hypothesis will have to remain as such and cannot be accepted as a valid theory. Even if such proof cannot be found, it would not detract from the empirical value of the practical use of dreams in each case. But the scientific significance would remain questionable until such proof is found. In the article referred to I undertook an experimental investigation of one of these concepts, namely, the relationship of recent impressions (*Tagesreste,* or the events of the day preceding the dream) to the dream itself as well as to the total personality of the subject. This was done by subjecting a series of persons to standard situations (pictures), recording their reproduction of the details and then searching in the dreams following the experiment for details that were left out in the reproduction. The results were highly gratifying in that I found that a relationship of this type can be proved to exist in the usual experimental way. A number of details that were left out in the reproduction of these pictures appeared in the dreams of the patients, and it was furthermore shown that the omitted details bore a definite relationship to the life problems of the patient. These details, then, that were "forgotten" by the patients had apparently been perceived and stored up but were not reproduced.

2. Malamud, W., and Linder, F. E.: Dreams and Their Relationship to Recent Impressions, Arch. Neurol. & Psychiat. **25**:1081 (May) 1931.

It was logical to assume that, because of their relationship to certain repressed trends in the minds of the patients, the details too were repressed and came out in the dreams along with the other repressed material that they were related to. During my experimental investigation of this particular aspect of dream psychology my attention was drawn to two other aspects which were equally important and which were also capable of experimental analysis. In the present article I shall report the results of further investigations undertaken which were primarily for the purpose of testing the validity of the results of the previous work and also a study of two additional features that came to light. The importance of these findings and their bearing on dream psychology can probably be best understood from the material that we have obtained, and for that reason it was decided to proceed directly with the presentation of the cases studied. The first of these is one in which all the factors are so clearly shown that it can be taken as representative.

Case 1.—I. G., a single woman, aged 29, was admitted to the hospital for treatment for severe stuttering associated with pronounced depression and suicidal tendencies. An analysis was undertaken, and among the chief factors that came to light were the following: In the family history there was a definite tendency to morbid depressions. The patient's father had committed suicide in an attack of depression, and on both the paternal and maternal sides of the family there were instances of maladjustment on the basis of psychopathic trends. The patient grew up in a home environment characterized by difficulties between the father and the maternal side of the family, with a great deal of quarreling between the two sides. Five brothers of the patient died in infancy, and the patient was brought up as an only child. Even as a child she showed pronounced tendencies toward a pyknic physique and experienced gradually increasing feelings of inferiority because of her unusual physical make-up. The earliest memories showed a marked attachment to the father. The feelings toward the mother consisted of a mixture of antagonism and admiration, with a tendency toward identification. She was breast-fed for only a few days, following which she was fed by bottle; this continued until she was about 2½ years old. At about the age of 2 she showed a marked interest in smoking, and shortly after that age she began to smoke cigaret butts and took an occasional puff at her father's cigars. He did not discourage her in this practice until the age of 5, when the habit reached such alarming proportions that the parents decided to stop it. When the opportunities to smoke were denied her she began to compensate by searching for objects used by the father for drinking and other purposes and would hold them in her mouth to obtain the satisfaction of the taste of tobacco left on them. This lasted until the age of 10.

An experience which she remembered vividly and which caused a great deal of distress to her was one in which she witnessed her father kissing the breasts of her mother, an action which at that time she interpreted as identical with nursing. This happened at the age of 3. From then up to the present she retained a marked aversion to such activities, feeling that this was one of the most abhorrent of perversions. The mother died when the patient was 12, and from then until her entrance into college at the age of 17 she was in very close contact with the father, showing a marked attachment to him and imbibing from him his views on the futility of life and the advisability of ending it by suicide.

Of further importance were the views against marriage that were imparted by the father. He went to all extremes to prove to her that it was a very objectionable experience and refused to allow her to have anything to do with men. At college she became acquainted with a man who was several years her senior, and whose disposition was much like that of the father. She gradually fell in love with him and became engaged to him much against the desires of the father. Four years before her entrance to the hospital this man committed suicide, possibly on the basis of a depression. This turned the patient back to the attachment to the father. Both now had the memories of their losses and would indulge frequently in mutual commiseration and discuss the advisability of committing suicide. Two years later the father, who had in the meantime gone into a deep depression, ended his life by shooting himself. Shortly after, the patient, who had already suffered a series of depressions, gradually began to stutter, which was the immediate reason for her admission to the hospital.

During the period between the development of these symptoms and entrance into the hospital she had shown a marked aversion toward association with men, and had experienced a series of pronounced attachments to women. Of further interest is the fact that from the earliest days of school life she had shown a marked interest in languages, and at college she took up the study of philology. Her interest in this subject was particularly significant, as it was marked by a great attachment to words as such. She loved words, especially those that would give her a certain rolling sensation as she pronounced them, and in her dreams she frequently saw herself slowly pronouncing these words and visualized the sounds as emanating from her mouth in the forms of beautiful round objects. The stuttering, which was very pronounced, was also characterized by the tendency to use words of this type and roll them in her mouth and on her lips for as long as she could.

During an early stage in the analysis and at a time when superficially she showed marked resistance to the analyst and the analytic situation, stating that she had no hopes for any success from the treatment and that she abhorred the analyst, the following experiment was undertaken. The picture of the Madonna nursing the child (fig. 1) was shown to her, and the procedure described in the previous article was followed. In her reproduction of the picture she gave a detailed description. She noted the mother and the baby as the high points in the picture, described minutely the baby's body and arms, the mother's clothes and the background, stated that she did not like the expression on the mother's face and added the existence of an outbuilding in the background, a bridge across a stream and a bundle of hay dragged by a man. She failed to state that the baby was nursing and did not mention the pillow and clothes under the baby. The next morning she said that she had had the following dreams:

First, she was in a dark room in the basement of the hospital. On the walls were large rats, toads and other vermin. The rats bit her. A "rectangular some thing" with a mouth at each end flattened itself against her and sucked blood from her. It hurt and burned, and she thought that her mother had set this thing on her. Then she was in a large building, sorting the clothes of a dead relative. They were a woman's clothes. She left the room, and someone stole the clothes. Then she was in her home town, and the father lay dead with an ugly hole in the abdomen. She dragged him into the house and placed him in an elaborate black coffin. Following this, she called the undertaker, saying that she was not sure whether her father was dead but she wanted to know whether she

should use embalming fluid on him. When she returned she found that the father was really dead, and that, in addition to his coffin, there was another one containing the mother. She entered the third room, and in it she met the man to whom she had been engaged. They walked down the road and came to a place with trees and a stream with a bridge across it. As they neared it she saw her mother crossing the bridge. The mother was not dead but was horribly disfigured. The left hand, the left side of the face and the breast were missing.

In the next dream the patient was in a large building again; the analyst was standing by a table; he handed her a letter which read, "Since all life is nothing but futility there is only one thing for us to do, and that is to amuse ourselves the best we can. Höchstachtungsvoll—." It was signed with the analyst's name; the analyst did not look as he did in actual life but resembled her father. The analyst disappeared, and the patient was driving a car down the street. There was a red brick house which she identified with a house in her home town. In

Fig. 1.—La Vierge au Coussin Vert, by Solario. (From a painting in the Louvre Museum, Paris; photograph by A. Bourdier, Versailles, France.)

it was a tall window, with curtains which had knots tied about them, which in her dream she recognized as the knots and tassels in the picture, which she had not described. She drove down the road and in crossing the railroad track was struck by the engine of a freight train. The car was demolished, but she was not hurt. Then she was back in the hospital hunting for the analyst and "wanting him very much without knowing why." Then it was night again; she was in bed, and something was smothering her. She became panicky, felt the blood throb in her face and neck and finally woke up.

Comment.—Before continuing with an analysis of the findings in this case as well as with the subsequent cases, two points relative to the technic should be emphasized: 1. The experiments were carried out by four investigators, although the cases were analyzed by myself. The reproduction of the stimuli presented, the recording of the dreams and the analysis of the relationships between the two were, therefore, obtained by observers who were not engaged in the analysis. 2. The experiences in the life of the patient that were secured in the analysis and that

seemed to be closely related to the series of dreams were obtained by the analyst through free association on these dreams. The interpretation of the dreams, therefore, as they appear in the following analysis, was made possible by the subsequent information given by the patient, although this information was called forth by the associations on the contents of the dreams.

The first and most striking feature in the result of this experiment is the definite relationship that the experimental situation bears to the dream. As in the cases reported in the previous article, one finds first that a number of features in the picture were distorted in reproduction. Some details were omitted and others were added, and both the omissions and additions, as well as the general tone of the picture, seemed to be definitely related to the series of dreams that was obtained. Furthermore, it would seem that these distortions, as well as their recurrence in the dream, bear a close relationship to the life history of the patient and the problem that formed the controlling feature of the disease. One sees that the conflicting attitude of the patient toward oral sensations, which was related to the irregularities of early feeding, the smoking and its interruption and especially the witnessing of the scene between the parents, showed itself in her failure to reproduce the most apparent feature of the picture, that is, the baby's nursing. The part of the mother's clothing and the pillow with its tassel on which the child is lying are omitted, as well as the description of the left side of the face and the left arm and hand that are particularly related to the act of nursing. In the dreams, on the other hand, throughout the whole series there was a constant recurrence of these features, even though in somewhat disguised form. The series opens with the patient being attacked by animals which bite and suck her body. The mother was in some way responsible for this, and the patient brought up in another dream the tassel and the curtain-like folds of the clothes under the child; even in her dream she had the feeling that they were parts of the picture which she did not reproduce. The breast, arm and left side of the face of the mother, which were omitted in the patient's description of the picture, were brought up in the dream but under the concept of mutilation. Some of the features which she added in her description also occurred in the dream in close relationship to her mother. Thus, the bridge which she placed in the picture appeared in the dream, and it is across this bridge that the mother approached. The man she saw in connection with this bridge appeared in the dream in the form of her fiancé. These relationships do not seem to be merely accidental but represent definite factors in her life that were closely connected with the problems that seemed to be instrumental in the cause of her difficulties. The strong oral erotic complexes which ran through her life and showed themselves in various forms, but which were repressed and came out only in her analytic associations, showed themselves in a repression of the features of the picture which were most closely associated with this function; but in the dream they overcame this repressive force and came out on the surface. The manner in which they came out, however, and the additional factors which they brought up with them in the dream show an orderly sequence throughout the series of dreams which throws a great deal of light on the mechanisms of the development of the condition as well as the manner in which they are related to it. The dreams open first with fear and aversion toward the act of sucking. It was in association with the analysis of this dream that the patient first brought up the fact that her earliest memory of such activity and the one that seemed to have been responsible for the development of her antipathy was the incident in which she saw the father kissing the mother's breast. During the subsequent analysis it was discovered that the feeling of abhorrence was definitely related to a feeling of jealousy of the mother, who was thus able to keep the

attachment of the father; the child felt herself inferior because she could not offer the same type of pleasure to the father. In the dream, however, the rôles are reversed, and the patient was the one who was being subjected to this attention, i. e., she took the mother's place (thus also reversing the situation in the picture), and, in fact, it was the mother herself who set this "rectangular something" on the patient. This sensation, however, was a painful one. She was being hurt and did not particularly desire to keep this type of relationship with the father. In the next two dreams two further steps were undertaken, with the result that both the father and the mother were dead and in coffins. Following this, in the fourth dream, the picture changed, and she found herself with the man who won her interest and attachment away from the father but whom she could have possessed only if the father and his objections were out of the way. At this point the mother too came into view. While the patient was strolling with this man and they were about to cross the bridge she met the mother. The mother, however, had lost that part of her anatomy which, in the picture as well as in the early experience of the patient, seemed to have been the most prominent characteristic of her ability to hold her place as a mother and wife. Next came the dream in which the patient went through the fulfilment of the wish which was paramount in her life following the loss of both father and sweetheart, that is, the attempt to commit suicide and thus escape the necessity of facing the difficult situation. This, however, ended with her being left unhurt. Then, through the process of reenacting the present situation by bringing in an actual item in the picture as well as the analyst, she bridged the gap and came to the present state of affairs. As has been mentioned, this was done when she still consciously felt and expressed an attitude of objection to both the analyst and the analysis. Under the surface, however, as is shown by the dream, this attitude had actually changed. The analyst appeared in the disguise of someone who looked like her father, and he handed her a letter which served two purposes: the linking up with the father's teachings and yet the promise of a new and pleasant future. The letter opened with an expression which she distinctly remembered as having often been used by the father —that life is nothing but futility. In signing the letter the analyst put down before his name the German expression which the father, who was German and who used to write to the patient in German, used frequently. The last sentence in the letter, however, was a distinct departure from the father's teachings: "There is only one thing for us to do, and that is to amuse ourselves." The analyst then disappeared, and she searched for him all over the hospital because she "wanted him very much." The final climax in the dream was represented in a picture which she herself in associations recognized as being of sexual significance.

Two features of importance can thus be seen to run through the series of dreams, in addition to the one brought out in the first article. The first feature consists in the relationship of one dream to another, causing them to act in a supplementary fashion. Each dream in itself, even though it represented a wish fulfilment which was related both to the life of the patient and to the stimulus presented to her, dealt with only a single problem in her life. The first dream is symbolic of her taking the mother's place; the second, of getting rid of the mother, and the third, of ridding herself of the father so as to obtain the freedom of association with her fiancé in the fourth dream. The fifth dream seems to do away entirely with the mother in such a way as to render her innocuous in her rivalry with the patient. The last dreams are all associated with bringing the patient across the gap of an unfortunate situation in which she lost both the father and the fiancé to an attachment to the physician, which was gradually beginning to materialize. This sequence of events, manifested through the series of dreams,

shows that in order to understand the problems and occurrences in the life of the patient one must obtain not only a single dream but a series of dreams which are representative of the different obstacles that the patient has to meet in order to adjust herself in a satisfactory way.

The other feature which is of importance is the insight which a study of this type gives into the nature of the relationship of the patient to the analysis and the analyst. On the surface the patient was still resistant to both. At one time she stated that she thought that very little could be accomplished by treatment because she had no respect for, faith in or any kind of attachment to the analyst. The experimental situation, in stimulating a series of dreams which expressed the underlying subconscious desires of the patient, proved this to be false and showed that in actuality the patient had already transferred her attachment to objects that she had lost to the physician and that she had the feeling of hope of a successful adjustment to life. Subsequent analysis proved these points to be borne out in fact.

The importance of these data from both a clinical and a psychopathologic point of view can hardly be overemphasized. In a satisfactory experimental way one can force a great many clues to come to the surface, but these clues, in order to give a consistent and systematic understanding of their relationship to the patient's difficulties, must be studied in a series of dreams rather than in only one dream. Furthermore, this method gives an insight not only into the problems of the patient but also into the attitude which she had taken toward the analysis and the physician who was treating her. That this is the case not only with one person but that it can be reproduced in others was shown by similar experiments with other patients.

CASE 2.—N. S., a married woman, aged 46, came to the hospital because of a severe neurosis that had developed during the year preceding admission. It was characterized by obsessive thoughts of injuring her husband and a grandchild who was living with them. Under analysis, some of the chief factors obtained were as follows: The early home environment had been unsatisfactory, particularly because the father was weak and submissive; he was older than the mother, who was of a domineering and active nature. The mother was the ruling element in the house and had always expressed dissatisfaction with the husband and his attitude. The patient was much attached to an older brother, who was much like the mother, a robust, active and domineering type. Early in life there were a number of sexual experiences with this brother, which were kept secret from the parents. These had always given the patient a feeling of guilt, but at the same time there was a craving for gratifications of this type. The family was poor, and the patient had to go to work at the age of 12; she continued working until marriage. Throughout this period she had a number of unfortunate sexual experiences, the first at the age of 14, which culminated in pregnancy and induced abortion. From then until marriage at the age of 22 she had had a number of such experiences and was subjected to severe punishment by the mother. All were kept under cover, and the last one, which also resulted in pregnancy, led to a forced marriage to her present husband who was, however, not the father of the child. The husband was ten years her senior, of a type much like her father, and was of a weak and unsatisfactory make-up sexually. The patient had very strong sexual drives and all through her married life was dissatisfied with the husband but never expressed these dissatisfactions. There were two children. The older, a girl, much like the patient, had also started in on a sexually active career early in life; her first child was illegitimate and led to forced marriage with a man who was not the father. The patient had always felt that this grandchild was a living proof of and punishment for her own sexual irregularities. At the same time she was greatly attached to him, at least superficially. Both the daughter

and her husband had developed a hatred toward this child, and the patient had taken the child into her home and had brought him up. It was this child, in addition to the husband, who was the object of her obsessive wishes to kill. Early in married life a brother-in-law of the husband had come to live with them; he was much like her own brother and mother. An attachment to him soon developed; at the same time the patient had fears that he might assault her sexually and kept entreating her husband to get rid of him. He finally did so. Following that, the patient made a superficially satisfactory adjustment to the situation. Shortly before the onset of her neurosis she began to have irregularities of menstruation and a gradually increasing sexual drive; at the same time the husband's sexual potency began to decrease, and thus a marked discrepancy resulted. It was at this time that the child came to live with them; he served as a constant reminder of her early sexual irregularities as sins as well as gratifications of her strong sexual desires. A series of incidents took place in which attachments to several men in the neighborhood developed; at the same time she felt a strongly increasing dissatisfaction with her husband. The culmination came with two incidents: In one, there was an assault by a woman on her husband, who took refuge in the house of the patient; in the second, another woman became insane and killed her child by slashing his throat. The patient had always had a tendency to be interested in morbid occurrences of this type and began to think how dreadful it would be if she were to become mentally deranged and do such things. On the morning when the man who was attacked by his wife took refuge in her house, the patient was listening to a tune over the radio, which had been a favorite of the husband's brother-in-law who had lived with them early in her married life. She suddenly became conscious of a feeling of weakness and confusion; she came out of that with the gradually developing obsessive ideas of killing the husband and the grandchild.

Early during her stay in the hospital, the patient was shown the picture by Cezanne (fig. 2), in which Medea is shown sitting on a rock with her two children in her arms and a dagger in her left hand. The patient described this picture rather poorly; she brought out a great many details of the background, but the controlling feature of the picture itself was hazy. She thought that a giant was sitting on an animal; he had a sword in his hand. She failed to mention the children. Following this she had a series of dreams. First, she saw the little boy (the grandchild) playing in the yard. Suddenly a woman stepped out from the background and began to chase the boy. The woman had a weapon in her hand which the patient did not see clearly, but she associated the woman with the neighbor who had become insane and had killed her child. Then she was at home. Her husband and a number of men were sawing wood. She went out and put her arms around the husband's neck and kissed him. The husband was angry and asked, "How many times do you want to kiss me?" In the next dream she saw her husband pack his things preparing to go away. He would not tell her where he was going. Then the little boy came up, and the husband took him and started to go away with him. Suddenly everything changed into a fire, and the house, along with the husband and child, seemed to burn up. In the next dream, she saw her husband and herself at home. The house caught fire. The husband rushed into the house to put the fire out, and that was the last she saw of him. In association with this she brought out spontaneously an incident that had happened a few months before she came to the hospital, in which the barn had caught fire. As the husband rushed in to save an animal, a falling timber hit him, and for a while the patient thought that the husband was killed and would burn up. Following this she dreamed of herself, her husband and the little boy riding in a

car which was going up-hill. The husband was driving, but try as he would he could not "make the hill." On top of the hill were her sister-in-law and her brother (it was in association with this that she brought out the experiences with this brother early in life). The brother came down, got into the car and drove it up. In a following dream she was alone in the yard, sitting with a pail of water. Her brother came and dipped his hands into the water and began to wash them. She was indignant and asked him whether he did not know better than to do such things.

Comment.—Here again one sees results similar to those in case 1. The picture (which is definitely related to the problems uppermost in the mind of the patient at the time of her disease) is described in a characteristic way. She left out all details that were definitely related to her own life. Medea is described as a man,

Fig. 2.—Medea, by Cezanne. (From the book on Cezanne by Julius Meier-Graefe, published by Ernest Benn, Ltd., London; Charles Scribner's Sons, New York.)

and the children are omitted from the picture. In the dream the omitted details appeared in the form of her grandson being chased by a woman with a knife in her hand and, judging by the associations, with the intention of carrying into effect the obsessive thoughts of the patient. This, however, is not all. The first dream set into action a chain of other dreams which, on the one hand, are indicative of the mechanisms underlying the production of this first dream, and, on the other, give an insight into the occurrences in the patient's life which led to the development of the disease. First was the depiction of the situation as it was, the husband refusing to grant gratification of her desires. He became angry when she kissed him and wanted her to stop. Next was the first attempt at a satisfactory adjustment; the husband was planning to remove himself and the boy, who was the reminder of her earlier indiscretions. This apparently was not drastic enough, so that at the end of this dream and in the next dream she relived an actual situation which almost succeeded in freeing her from an unsatisfactory husband:

The husband and the child both burned up in the house. With this obstacle out of the way she reverted to a situation in early life, in which the brother took the place of the husband and drove the car up-hill, substituting for the husband who could not do it. Whether or not one accepts the rather tempting interpretation of the car and the hill in a symbolic fashion, one cannot help realizing that the patient had always yearned for a strong hand to take care of her in real life in a manner which the husband could not do and that in searching for such a person she naturally reverted to the brother who in early life represented to her the masculine characteristics which she did not find in subsequent life. A similar incident, with symbolic significance, was depicted in the last dream. It is interesting that in the patient's associations on this dream she stated that the brother did not look quite the same as he did in actual life; she associated him with the physician who was taking care of her during the early months of her illness, a man of a domineering and decisive nature who had tried to intimidate her into dropping her neurotic manifestations. She added that this man would have been successful in helping her a great deal if it were not for the fact that he had tried to dominate her too much and accomplish a cure by intimidation. She felt that the treatment of the analyst had this characteristic of force and instillation of faith, but that it had the additional value of sympathy and understanding. One sees here, then, throughout a series of dreams, an attempt to deal in a direct manner with the obstacles as the patient saw them in her way; not all obstacles were indicated in any single dream but were revealed in a continuation of the series. Furthermore, early in the analytic treatment she had indicated the beginning of transference to the physician and the transference of her attachment to the brother through the outside physician to the analyst.

Case 3.—In this case the experiment was carried out in a somewhat singular fashion. D. D., a single man, aged 33, came to the hospital because of hypochondriacal trends and feelings of inadequacy, which had developed during postgraduate study at a university. He had graduated from a school of architecture at the age of 22 and had taken a position in a large firm. At first he had made a fairly successful adjustment, but he did not gain as rapid promotion as his fellow workers. With the general economic depression he lost his job, and, having no prospects of another, decided to go to the university and by taking a postgraduate course increase his opportunities for a better position. He was the son of a successful man who had saved some money, and who now, in his old age, had retired from business and was willing to help the patient in his new venture. From his earliest years the patient had been rather asthenic. He was introvertive and given to day-dreaming and had little initiative. He had always had high ambitions but had never had the competitive spirit and energy necessary to carry them into effect. The father in earlier days had been a successful business man, and the patient had always felt himself inferior to the father and incapable of forming any close relationship to him. The father was strict and exacting. The mother, on the other hand, was much like the patient and had always intervened in his behalf whenever any kind of friction had developed between the father and son. During the last few months the patient's father had had a series of strokes, presumably due to arteriosclerosis, and the patient (having throughout life secretly identified himself with the father and wished to be like him) now lost all hope for a successful future; he felt that his physical disorders, headaches and the like, were probably indicative of beginning arteriosclerosis which he had inherited from the father, although he presented no signs of this or of any other physical disease.

Early during the analysis the patient described several dreams of the preceding night. In trying to ascertain what the occurrences in the last few days had been

that might have served as the recent impression for the dreams, it was learned that on the previous afternoon the patient had seen a motion picture. He stated, however, that he was much worried during the show and did not remember any of its details, although he remembered the name. The plot of the picture, as was afterwards learned, centered about the struggles and vicissitudes encountered in the life of the hero, who, in the face of difficulties, by virtue of indomitable courage built up a successful career culminating in the crisis of a national depression. Early in life, following a financial disaster, he left home with his bride to seek his fortune; on the way they were attacked by desperadoes who shot and wounded him in the left shoulder. In spite of the serious illness that followed, he carried on and built up a successful business. His daughter married a weak type of man who failed to stand up under a subsequent financial crisis, but the grandchild showed much of the spirit of the grandfather and succeeded in a similar fashion. In the final crisis of the picture it was the grandson who, in spite of the objections of the old man, sacrificed the fortune he had amassed in an attempt to save the standards built up by the house. All that the patient remembered of the picture was that a young man was faced with a series of difficult situations in which he had to undergo a number of trying experiences, but he did not know exactly what they were.

The dreams were as follows: In dream 1, he went to a motion picture theater and bought a ticket, with the understanding that he could see the last part of the matinée and the first part of the evening show. The picture was the one which he had seen, but he had two engagements, one in the early afternoon and the other in the late evening, and it was because of this that he wanted to make the arrangement suggested. For this purpose he had to have the usher give him a return ticket so that he could come back to the evening performance. The usher claimed that he did not have the authority to do so and referred him to the manager. The latter refused permission and they entered into an argument. It ended in his not being able to convince the manager of the justice of the arrangement, and the patient became angry and left without seeing the picture. In associations, he first brought out that the manager did not look like the actual manager of the theater but resembled a professor at school who had been particularly strict with him and who, on several occasions had told him that his work was not satisfactory and that he was disappointed in him. The man in the dream, however, was older than this professor and reminded him to a certain extent of his father, especially in his strict and unyielding nature. The second point was that he actually had seen this picture at the matinée and that no such arrangement as was depicted in the dream was necessary. In dream 2 he saw himself in the classroom which was peculiar in that it had two levels much like the balcony and orchestra of a motion picture theater. He was sitting in the orchestra under the balcony with his back to the place where the screen is situated. Someone had called to him to get up and recite. As he arose and was about to turn around everything went black before his eyes, and he stiffened and went into a convulsion. In association he brought out an incident he had witnessed in early life in which a boy sitting next him in a schoolroom was called on to recite a difficult piece. The boy was frightened; he fell and went into what the patient was told afterward was an epileptic convulsion.

In dream 3 the patient was returning home with a girl; he stopped in front of a house and intended to stay in the car for a short while with the girl. A man suddenly appeared and poked a pistol at him. The patient told the girl to run, and while she did so the patient lunged at the man's knees. The man shot at him; the bullets entered his body, but they did not hurt him. In dream 4 he was in his

father's house with an elderly lady. The door opened, and he saw at the top of the stairs a bear, which tried to force its way into the room. He slammed the door to keep it out and then tried to escape through the window, but as he looked out the window he saw a man leading the bear up the street by a rope attached to the animal's neck. The bear walked upright as though it were a man. In association, the patient described an experience in which his father had frightened him by putting on the hide of a bear. The man leading the bear was a neighbor who had been kind to him in early life. In dream 5 he saw himself in his home; his father had just had a bad fall and was confined to bed. He had a feeling of pity for the father and at the same time a feeling of growing strength within himself as he considered the necessity of having to take care of his mother now. A physician was called in and said that the father was hopelessly insane and would have to be taken to a state hospital. Following this, the patient had dream 6, in which he was in his parents' home. There was a bed in a dark room. As the dream opened, he was in the center of the room; he had just risen from a bed in the rear of the room. He walked toward the bathroom to get a drink when he saw a man sleeping on the floor in front of the bathroom door. This man was his father; to get into the bathroom he would have to disturb him and run the risk of waking him up. Somehow he found himself in the bathroom, and while he was engaged in looking for the faucet a man rushed in and was about to attack him. He picked up a chair with which to defend himself, but the next moment he found himself back in the original room with his mother, who was sitting on the bed dressed in night clothes. The man had disappeared and so had the father.

In the last dream he saw himself in an assembly hall; there was a large crowd, and he felt himself above the others, as though he were superior. He felt as though he were expected to perform something unique and as though the crowd expected him to do something; he was a bit frightened at the responsibility. He looked across the room and saw the analyst gazing at him with approval and encouragement and felt much reassured.

Comment.—Here, too, is an experimental situation which in its results is similar to those in the two previous cases. The picture that supplied the stimulus was not experimentally presented to the patient but was experienced shortly before the dreams. It is important to appreciate that the picture and the occurrences in it were closely related to the patient's own life problems, except that in the picture the situation was reversed. In the patient's case his forbears had been successful and strong; he could not bring himself to do the things which would keep the family tradition at its proper level. In the picture, however, the last link in the family chain proved to be strong and showed ability to carry the load of the difficulties. The man in the picture had succeeded in doing what the patient always had wanted to do but had lacked the ability to accomplish. In recounting the picture the patient missed all the details. In the first dream he dealt with a superficial problem in his life which he was apparently experiencing at the time, that is to say, the picture itself. He succeeded in creating a situation which did not permit him to see the picture and undergo the humiliation of admitting to himself that he was incapable of doing the task which the man in the picture accomplished. The responsibility for this was shifted from the patient to the father and the father-image in terms of a professor. Dream 2 shows another method of escape from the necessity of facing a difficult task. He reverted to the method employed by the pupil, which had proved successful in saving him from reciting at school. Following that, in dream 3 he drifted back to earlier dreams and fantasies in which he used to see himself growing up to be a successful man much like the man in the picture. The identification with the strong founder of the family is

first indicated by the experience of being attacked by the ruffian and shot in a manner similar to that in the picture. Dream 4 dealt with the removal of the threatening influence of the strict father, picturing this influence as a danger to himself in the form of a bear. In dream 5 he assumed the position of the younger man in the picture, who had to step in to take the load off the shoulders of the aging man. In this dream the father was sick, "hopelessly insane," and the patient had to take matters in hand and look after his mother. Following this, in dream 7 there was another attempt to remove the father, but this time as the rival in obtaining the mother's affections. In the last dream the patient attained success and was at the head of the multitude; his feelings of inadequacy and lack of ability to deal with the situation were counteracted by faith in the help that the analyst could give him.

ADDITIONAL EXPERIMENTS

In case 3 it is seen that the stimulus in the experimental situation need not be in the form of the pictures used in the experiments described in the first article. Any controlled situation in which the stimuli are known can serve as a starting point for a series of dreams. In a number of additional experiments I tried a new arrangement in this procedure by substituting a literary passage for a picture. This passage was taken from James Branch Cabell's book "Jurgen."[3] The passage used is a synthesis of several paragraphs in the book. As the book and its characters are well known, it was thought advisable to substitute fictitious names for those given. The passage, as presented to the subjects, read: "Helen had half opened the door of her bedroom and, with a lamp in her hand, was peering out into the narrow stairway. Richard was embarrassed to find himself, at this hour, in the presence of this beautiful, dark woman, under such intimate circumstances. He rose to his feet and hastily put up the weapon that he had exhibited to Queen Sylvia and decided to pass airily over the whole affair. Outside a cock crowed, for it was dawn. They left the dark passage and went forward across the beach, through sand hills to a moor, seeing no one and walking in a gray fog. They passed many gray, fat, sluggish worms and some curious gray reptiles. Then they came to a wall that was high and gray, and to a door that was in the wall."

This literary production was presented to the patients in a manner much like that followed in showing the pictures. The patient was placed in a quiet room. The physician engaged the patient in conversation on an indifferent topic, and then the patient was given the passage and was told to read it aloud and try to remember the details so as to be able to reproduce it. When the patient had finished reading, the typewritten page was taken away; after five minutes of further conversation on an indifferent topic the patient was asked to reproduce what he had read; a verbatim report was taken of this reproduction. Here, as in the case of the pictures, the reproduction, although varying with different patients, had one common characteristic: some of the details were distorted. The patient was then told that if he had any dreams that night he should tell them to the physician. The results were similar to those obtained with the pictures, although the effect was not as striking; apparently the reading of the passage was not so strong a stimulus. A number of patients were subjected to this experiment. The details most frequently omitted in the reproduction of the passage (especially by the female subjects) were the exhibition of the weapon, the reptiles and the worms.

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3. Cabell, J. B.: Jurgen, New York, Robert M. McBride & Company. (For permission to use the passage from Jurgen and its reproduction in this article I am indebted to Mr. James Branch Cabell.)

Frequently the male subjects substituted "gun" for "weapon," using such phrases as "he drew his gun at the woman," "he shot at the woman with a gun," and similar expressions. In a number of cases the names of the participants were replaced by names of friends or relatives. The details thus distorted recurred in a number of cases in the dreams following, sometimes overtly and at other times disguised in symbolic fashion. In all, the details were woven into the structure of the dreams and were definitely related to the life problems of the patients. I propose at this time to give only a few examples of the results obtained.

CASE 4.—A married woman, aged 37, with a condition diagnosed as psychasthenia, had obsessions (thoughts of contamination) on the basis of early psychic traumas and an unsatisfactory marital situation. In reproducing the passage she left out the exhibition of the weapon and the door in the wall. In her dream she was hiking "some place" with her husband. They came to a barn through which they had to pass, but there was no door in it. The husband "broke down some of the planks" to allow them to get through. As they were climbing through this opening she noticed some clothes hanging on the wall. As they reached the other side she found a "knife with a cream-colored handle" that had apparently fallen out of the clothes.

In this case both the omitted details recurred in the dream and were found to bear a relationship to the following dreams in the series as well as to the problems involved in the mental disease of the patient.

CASE 5.—A single woman, aged 25, had a psychogenic depression, which had developed on the basis of an unrequited love affair. In the reproduction of the passage she left out the weapon, although the rest of the reproduction was exceptionally good. In one dream she saw the man she loved; he handed her a "cigar"; his face was turned away as if he were "embarrassed." It was a peculiar looking cigar, flat throughout its length but thick and knoblike at the end. Here, too, association brought out the relationships referred to.

CASE 6.—A single woman, aged 21, had a mental disorder diagnosed as a schizophrenic psychosis, which had been precipitated by a series of homosexual experiences with an older woman. In reproducing the passage she made no mention of the weapon but stated that Helen had a candle in her hand (instead of the lamp). In the series of dreams that followed, the woman who had played an important part in the precipitation of the psychosis appeared frequently. As the dream ended the patient was swimming in a lake with "someone else." This person disappeared; in her place was a snake swimming after the patient, and she was frightened.

GENERAL COMMENT

In the cases cited the results are representative of those obtained in a number of other cases. In some cases I attempted free association shortly after the exposition of the pictures or the literary passage. I could not, however, definitely substantiate the findings of Allers and Teller,[4] who found that in most cases the details omitted in the reproduction either did not appear at all in the association or were represented only in a vague symbolic fashion.

4. Allers, R., and Teller, J.: Ueber die Verwertung unbemerkter Eindrücke bei Assoziationen, Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:492, 1924.

In my study of the dreams, which followed the reading of the passage, the results were essentially the same as in the experiments in which pictures were used. Here, too, the stimulus offered by the controlled situation resulted in a series of dreams which presented the following features: (1) the recurrence of details omitted, added or distorted in the reproduction; (2) the manifestation of a progressive series of problems in the life of the person in the form of solutions for each of these problems in the gradual unfolding of the dreams, and (3) the indication of the patient's attitude toward the analytic situation.

The last two features in the analysis of dreams were also observed in a series of cases in which the dreams were obtained without the preliminary experimental situation. The absence of a known, controlled *Tagesrest* made the analysis more difficult and less clear. It was evident, however, that a study of a consecutive series of dreams rather than of isolated examples afforded readier insight into the different problems of the patient and helped materially in shortening the course of the analysis. In a number of cases, especially when the intelligence of the patient permitted, it was found helpful to have the patient realize the relationship of these phenomena and grasp their significance (as was suggested by Jung and Kranefeldt [5]). This was particularly useful in conditions other than psychoneuroses and when modifications of the freudian method were employed. In some cases various other modifications are necessary. These concern, first, the nature of the stimuli presented. As these stimuli are valuable only when they are related to problems or conflicts in the patient's life, it frequently happens, especially in new cases, concerning which one knows little, that the first attempt is not successful. In these cases one may have to try several different experimental situations. Furthermore, in obtaining a series of dreams one frequently has to take dreams which occur during two or more nights. Whether the series of dreams are of the same night or of several consecutive nights, one may sometimes secure a transposition of the order, as concerns the level of the given problems or their chronologic sequence. This must be borne in mind in analysis subsequent to the experiment. In all cases it is important to remember that the dreams should be used only as indicators of problems; interpretation can be undertaken only on the basis of subsequent analysis.

The value of an approach of this type lies in its usefulness both to the psychopathologist and to the clinician. To the former it affords a valid experimental method for the investigation of certain aspects of dream psychology; to the latter it offers a reliable instrument with which to investigate the mechanism of the disease.

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5. Kranefeldt, W. M.: Arch. f. Psychiat. **96**:219, 1932.

SUMMARY

The results of this investigation show:

1. As was stated in a previous article, it was found that details omitted or added in the reproduction of a given set of stimuli reappeared in dreams and that the details, as well as the dreams, were related to the problems in the life of the subject.

2. The dreams following the experiment, if taken in series, afforded clues to the different problems of the given subject, and subsequent analysis showed that the dreams represented the attempts of the subject to deal with these problems in a more or less systematic fashion.

3. The dreams also served as indicators of the attitude taken by the subject toward the analysis and the analyst.

MORPHOGENESIS AND EVOLUTION OF THE CEREBELLUM

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The morphology of the mammalian cerebellum has remained obscure in some important respects because of insufficient knowledge of the comparative anatomy of the organ. Advances in the knowledge of the structure and development of the cerebellum in amphibians and reptiles, together with a study of the organ, fetal and adult, in several mammals in which this part of the nervous system is relatively primitive, has thrown new light on important aspects of its morphology which have physiologic bearings. A summary of these comparative studies will be presented here.

The cerebellum of the fishes has been so well reviewed by Herrick [1] that there is little to add, save to make reference to the newer contributions of van der Horst.[2] These consist of an analysis of the cerebellum of the generalized lung-fish, Ceratodus, and of several Ganoidei and Teleostomi. Without going into details, it may be stated that, in general, the cerebellum of fishes falls into the same pattern of trigeminal and spinal corpus cerebelli and acousticolateral auricular lobe or eminentia granularis as does that of amphibians, as described in the following pages. There are, however, many features of the cerebellum of fishes which are puzzling when compared with the simpler organ of amphibians, and a close comparison will not be attempted.

The cerebellum of birds is also omitted from the present account. It has been thoroughly described by Brouwer and by Ingvar. In general the morphologic pattern is the same as that here presented for reptiles and mammals. There are differences of interpretation of some parts, as compared with the conclusions of Ingvar to which reference will be made in connection with the mammalian cerebellum. It must be recalled that the teleost fishes, especially, and the birds represent terminal branches of the phylogenetic tree which diverge from the mammalian evolutionary stem.

From the Anatomical Laboratory, University of Oregon Medical School.

1. Herrick, C. Judson: Origin and Evolution of the Cerebellum, Arch. Neurol. & Psychiat. **11**:621 (June) 1924.

2. van der Horst, C. J.: The Cerebellum of Fishes: I. General Morphology of the Cerebellum, Proc. Kon. Akad. van Wetenschappen te Amsterdam **28**:735, 1925. II. The Cerebellum of Megalops Cyprinoides (Brouss) and Its Connections, ibid. **29**:44, 1925.

AMPHIBIANS

Without reviewing again the fundamental studies of Johnston [3] on Petromyzon and of Herrick [4] on Necturus, I shall pass directly to a consideration of the embryonic development of the cerebellum in amphibians, and of its structure in amphibians, reptiles and mammals on the basis of studies reported in detail elsewhere.

In the larva of Amblystoma,[5] just prior to the early flexure stage of Coghill, there is found a group of cells in the alar plate of the region immediately caudal to the cephalic flexure which have assumed the aspect of the modified Rohon-Beard cells of Coghill. Their subsequent history shows that they become cerebellar cells. Already some of these cells have short, ventrally directed processes. At this stage the cells appear to be migrating ventrolaterally. They extend as far caudally as the level of the fifth cranial nerve root, with a few similar cells opposite the entrance of the seventh and eighth roots.

At the early flexure stage the cell group (fig. 1 *a*) is much more prominent. The cells are large and rounded and, as a rule, have ventrally directed processes, but in the dorsal part of the group some of the cells send their processes dorsomedially. At this stage some smaller cells may also be recognized. One may now speak of a definitive anlage of the cerebellum. In subsequent stages (fig. 1 *b* and *c*), up to one day after the early swimming stage, there is rapid proliferation of cells and growth of their fibers, together with migration of some of the dorsomedially placed cells into the hitherto membranous roof of the ventricle at this level. During the first day after the swimming reaction has begun, fibers have grown across this dorsal plate in such a fashion as to form a commissure between the masses of cells of the cerebellar anlage on either side (fig. 2 *a*). This is the cerebellar commissure. Farther ventrally the cerebellar anlage has increased by proliferation of its cells so that a large cell mass, the corpus cerebelli, is recognizable. The commissure connects the two corpora cerebelli. The only cells present in the cerebellar plate near the midplane at this stage, and for some days subsequently, are ependymal cells. Presently, however, nerve cells migrate far enough medially so that the midplane region of the cerebellar plate also may be considered nonmembranous. Accompanying this migration of cells there is a marked downward arching of the zone joining the cerebellar plate and midbrain so that the rostrocaudal axis of the cerebellum comes to have a pronounced upward tilt (fig. 2 *b*).

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3. Johnston, J. B.: The Brain of Petromyzon, J. Comp. Neurol. **12**:1, 1902.

4. Herrick, C. Judson: The Cerebellum of Necturus and Other Urodele Amphibia, J. Comp. Neurol. **24**:1, 1914.

5. Larsell, O.: The Development of the Cerebellum in Amblystoma, J. Comp. Neurol. **54**:357, 1932.

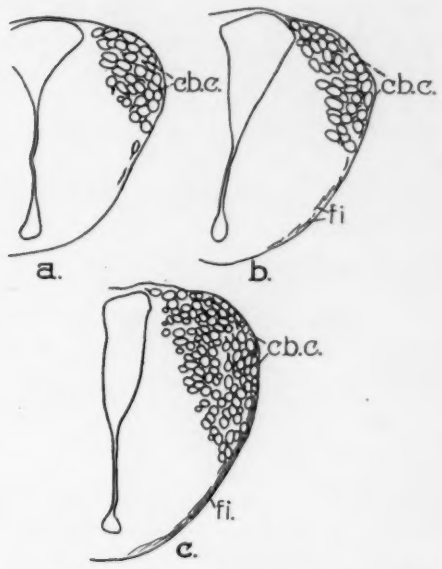


Fig. 1.—Cross-sections through the cerebellar region of larval Amblystoma, showing the group of cerebellar cells at several early stages: *a*, early flexure stage; *b*, coil stage; *c*, early swimming stage (slightly modified from Larsell, O.: J. Comp. Neurol. **54**:357, 1932); × 95. The following abbreviations are used in the figures: *a.ac.*, acousticolateral area; *aq.*, aqueduct of Sylvius; *br.conj.*, brachium conjunctivum; *br.pontis*, brachium pontis; *cb.c.*, cerebellar cells; *c.cb.*, corpus cerebelli; *co.cb.*, cerebellar (trigeminal) commissure; *co.lat.*, lateral (acousticolateral or vestibular) commissure; *d.a.*, anterior diverticulum of fourth ventricular lateral recess; *em.ch.v.*, ventral cerebellar eminence; *f.unc.*, uncinate fasciculus of Russell; *fi.*, nerve fibers; *fis.ppd.*, prepyramidal fissure; *fis.pr.*, fissura prima; *fis.sec.*, fissura secunda; *fis.un.*, uvulonodular fissure; *fis.x*, fissure x; *fis. y*, fissure y; *floc.*, flocculus; *hyp.*, hypophysis; *l.aur.*, auricular lobe; *lo.floc.*, floccular lobe; *lo.lat.cb.*, lateral lobe of cerebellum, i. e., cerebellar hemisphere; *lo.med.*, lobus medius; *med.obl.*, medulla oblongata; *mes.*, midbrain; *mes.V c.*, mesencephalic V cells; *n.IV*, trochlear nerve; *n.V*, trigeminal nerve; *n.VII*, facial nerve; *n.VIII*, acoustic nerve; *n.IX*, glossopharyngeal nerve; *n.X.*, vagus nerve; *nod.*, nodulus; *nuc.cb.*, nucleus cerebelli; *nuc.dent.*, nucleus dentatus; *nuc.fast.*, nucleus fastigii; *nuc.int.*, nucleus intermedius; *nuc.lat.*, nucleus lateralis; *nuc.med.*, nucleus medialis; *par.*, paraflocculus; *r.l.*, lateral recess of fourth ventricle; *r.V*, trigeminal roots; *r.V mes.*, mesencephalic V roots; *r.VII l.l.*, lateral line roots of seventh nerve; *rVIII*, vestibular roots; *r.X l.l.*, lateral-line roots of tenth nerve; *s.lat.*, lateral sulcus of ventricular floor; *s.par.*, sulcus parafloccularis; *s.pc.*, sulcus postcentralis; *str.gran.*, granular layer; *str.med.*, medullary layer; *str.mol.*, molecular layer; *str.Pur.c.*, Purkinje cell layer; *tela a.*, tela anterior; *pyr.*, pyramis; *tr.cb.teg.*, cerebello-tegmental tract; *tr.sp.cb.*, spinocerebellar tract; *tr.sp.cb.d.*, dorsal spinocerebellar tract; *tr.sp.cb.v.*, ventral spinocerebellar tract; *tr.v.cb.*, vestibulocerebellar tract; *tr.v.cb.d.*, direct vestibulocerebellar tract; *t.v.4*, taenia of fourth ventricle; *uv.*, uvula; *v.m.a.*, anterior medullary velum; *v.m.p.*, posterior medullary velum; *v.4*, fourth ventricle.

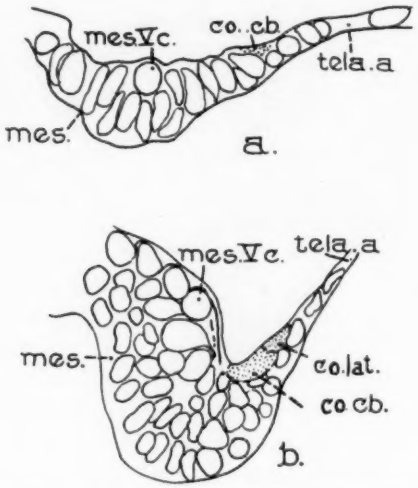


Fig. 2.—Sagittal sections through the cerebellar region of Amblystoma larvae: *a*, midsagittal section at 3 days after early swimming; *b*, slightly parasagittal section at the early feeding stage (slightly modified from Larsell, O.: J. Comp. Neurol. **53**:357, 1932); × 360.

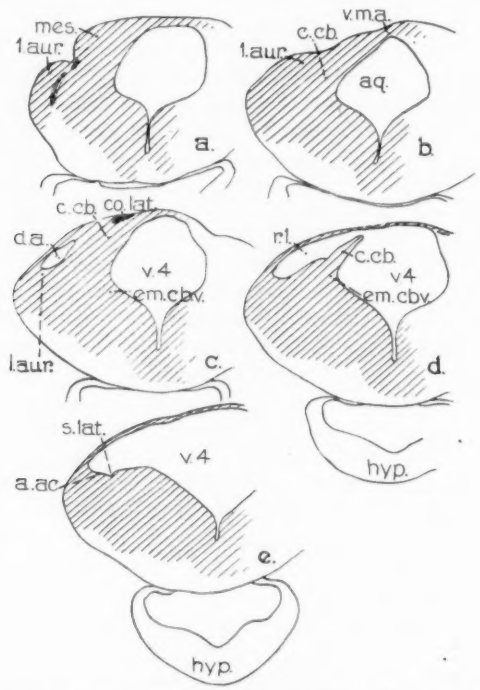


Fig. 3.—Transverse sections through cerebellar region of Amblystoma larva at 4 days after early swimming stage (slightly modified from Larsell, O.: J. Comp. Neurol. **54**:357, 1932); about × 50.

The mass of cerebellar cells increases rapidly, and by three days after the early swimming stage a lateral and slightly rostral projection beyond the general surface of the rostral end of the medulla oblongata may be recognized. This is the beginning of the auricular lobe (fig. 3). Caudally this lobe merges with the acousticolateral region of the medulla oblongata.

In the meantime a second commissure has been formed in the cerebellar plate, caudal to the first. This commissure, designated as the lateral cerebellar commissure (figs. 2 *b* and 3 *c*), is composed of finer fibers than the commissura cerebelli. It has its origin from cells of the auricular lobe and connects the auricular lobes of the two sides as the cerebellar commissure connects the two corpora cerebelli.

The auricular lobe grows rapidly, both in the lateral direction and rostrally, so that presently there is formed between it and the corpus cerebelli a blind pouch roofed over with membrane and continuous caudally with the lateral recess of the fourth ventricle (fig. 3 *c*, *d* and *e*). This constitutes the anterior diverticulum. Its floor is continuous medially with the corpus cerebelli and laterally with the auricular lobe. However, with continued growth of the auricular lobe rostrally, the diverticulum extends forward into the auricle, the upper surface of which forms the floor of the pouch. Its roof is formed by an ependymal membrane extending from the superior and rostrolateral margins of the corpus cerebelli to the lateral margin of the auricular lobe, but at the rostral extremity of the diverticulum its roof membrane extends from the medial margin of the auricular lobe to the lateral margin of the same; i. e., the medial part of the auricular lobe is a forward growth from the corpus cerebelli. The lateral part is more intimately related to the acousticolateral area of the medulla oblongata.

In the younger larvae which show the cerebellar commissure it is not possible to determine the exact position of the cells of origin of the commissural fibers. It can only be stated that these fibers come from the general region of the body of the cerebellum. In midlarval stages, however, in Golgi sections it is evident that the cerebellar commissure arises from cells in the lower part of the corpus cerebelli, adjacent to the superior trigeminal nucleus, and also from cells of the superior trigeminal region. Commissural fibers clearly terminate in the superior fifth nucleus of the opposite side. Direct trigeminal fibers also enter the commissure, as in other urodeles, so that the cerebellar commissure is largely intertrigeminal. Spinocerebellar fibers also enter it, but tend to form a bundle which is more or less distinct from the trigeminal and corpus cerebelli fibers.

The lateral commissure is made of much finer fibers than the trigeminal commissure and has its origin from cells in the rostral and

rostrolateral parts of the auricular lobe, i. e., in the acousticolateral correlating zone. It is in this region that the vestibular roots and the lateral-line roots have their rostral terminations (fig. 4). The lateral commissure must therefore be regarded as a vestibulolateral commissure, connecting the auricular lobes of the two sides, as the intertrigeminal and spinocerebellar commissure connects the corpora cerebelli. The fibers arise from small cells which resemble granular cells. The slender fibers themselves suggest primitive parallel fibers. Accompanying the fine fibers of the lateral commissure are also coarser direct vestibular root fibers which pass to the opposite side. These correspond to the direct vestibular root fibers described by Johnston in the cerebellum of Petromyzon.[3]

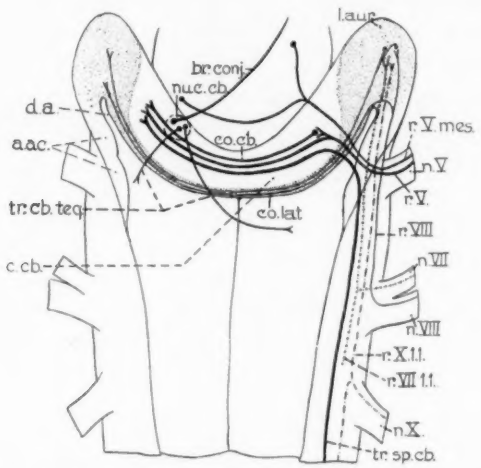


Fig. 4.—Diagram of the chief cerebellar connections in Triturus torosus. The auricular lobe is stippled.

In addition to the trigeminal fibers which enter the superior trigeminal nucleus and the neighboring region of the corpus cerebelli, spinocerebellar fibers from the cord also reach the corpus cerebelli. As already stated, some of these decussate with the cerebellar commissure. A tectocerebellar tract also enters the cerebellum from the midbrain, and there are evidences of a mamillocerebellar tract and of bulbocerebellar fibers. There are thus laid down in larval Amblystoma at the rostral end of the medulla oblongata two commissures which pass through the roof of the fourth ventricle and connect the two correlating zones established on either side, namely, the trigeminal and spinocerebellar zone of the corpus cerebelli, which receives also tectocerebellar and apparently mamillocerebellar fibers, and the acousticolateral areas, which receive vestibular and lateral-line seventh and tenth nerve fibers. Each

acousticolateral area is connected rostrocaudally by the correlating tracts *a* and *b* of Kingsbury.

After the commissures have bridged the ventricular roof, they are followed by nerve cells which migrate medially from either side, giving rise eventually to a relatively massive cerebellar arch (fig. 3 *b*). Some of these nerve cells differentiate into Purkinje cells; others remain as commissural cells and granule cells. At the walking stage of the larva the lateral commissure forms a definite although primitive molecular layer in the dorsocaudal part of the cerebellum. Ventrocaudad to this lies a mass of cells which represents the primitive granular layer, and scattered in the two layers are primitive Purkinje cells, their dendrites projecting into the commissural fibers.

A reduced cerebellar crest is present in the larva, continuous caudally with the fibrous zone of the acousticolateral area and rostromedially with the molecular layer of the cerebellum. There is also a gradual transition from the cells of the medulla oblongata whose dendrites spread into the acousticolateral area to the Purkinje cells of the auricular lobe and corpus cerebelli. The auricular lobe shows by the arrangement of its cells that laterally it is a continuation of the acousticolateral area, while medially it is continuous, and more closely related functionally, with the corpus cerebelli. Cells of both the medial and the lateral parts send dendrites into the zone occupied by spinocerebellar, spinotectal and ascending fifth fibers, thus indicating a functional unity of the two parts, but in addition the laterally placed cells of the lateral portion of the lobe send their dendrites into the rostral continuation of the acousticolateral area. There occurs thus within the auricular lobe a partial correlation of vestibular, lateral-line, trigeminal and spinocerebellar impulses. Correlation between spinocerebellar, trigeminal, tectocerebellar and possibly mamillocerebellar impulses must take place in the corpus cerebelli. Through the two commissures and the cells which have migrated along their course, further correlation between these two groups of partially correlated stimuli must occur in the arch of the cerebellum; i. e., the two chief kinds of stimuli, namely, proprioceptive impulses from the trunk and limbs and vestibular and lateral-line impulses from their respective organs, are correlated and coordinated in the suprasegmental structure which has grown about the commissures.

In adult Amblystoma [6] most of these features can be recognized, although those related to the auricular lobe are more clearly seen (figs. 4 and 5) in the adult newt, Triturus torosus.[7] The latter shows par-

6. Larsell, O.: The Cerebellum of Amblystoma, J. Comp. Neurol. **31**:259, 1920.

7. Larsell, O.: The Cerebellum of Triturus Torosus, J. Comp. Neurol. **53**:1, 1931.

ticularly well the relations between the cerebellar crest and the molecular layer of the cerebellum, and also between the lateral and medial parts of the auricular lobe, to the acousticolateral area and the corpus cerebelli respectively. Further details are given elsewhere.

In Triturus is seen the first evidence of an external fissure (fig. 5, *fis. un.*). This occurs in the form of a transversely directed groove on either side, marking the boundary of the vestibulolateral zone which is continuous with the acousticolateral part of the auricular lobe from the corpus cerebelli. It does not extend to the midplane.

In the developing frog the process described for Amblystoma, so far as it concerns all but the earliest stages of cerebellar formation, has been shown to be repeated,[8a] but in much abbreviated form. The auricular lobe and corpus cerebelli develop and fuse together as in

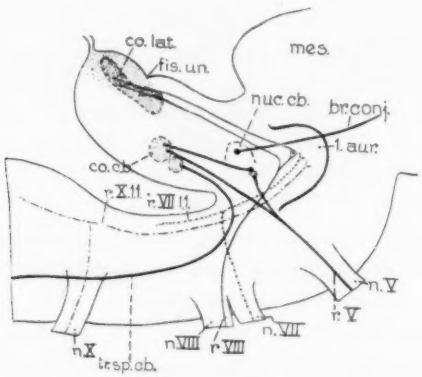


Fig. 5.—Diagram of the cerebellar region and some of the fiber tracts in Triturus torosus, as projected on the sagittal plane. The auricular lobe is stippled.

Amblystoma, but the auricle is relatively much smaller. With the degeneration and disappearance of the lateral-line organs, at the beginning of metamorphosis in the frog, the auricular lobe is reduced in size to a small lateral projection with only vestibular connections. In the adult frog the vestibular connections to the cerebellum are present in the form of both direct vestibular root fibers and a tract from the vestibular nucleus to the cerebellum. The auricular lobe is greatly reduced, consisting almost entirely of the floor of the anterior diverticulum which comes to the surface as the eminentia granularis, covered by a thin membrane. Fibers, probably direct vestibular fibers, pass dorsally from the region of the reduced auricular lobe, along the lateral margin

8. Larsell, O.: (*a*) The Development of the Cerebellum in the Frog (Hyla Regilla) in Relation to the Vestibular and the Lateral-Line Systems, J. Comp. Neurol. **39**:249, 1925; (*b*) The Cerebellum of the Frog, ibid. **36**:89, 1923.

of the cerebellum, to turn medially and decussate. They appear to correspond with the lateral commissure, and were so designated in an earlier paper (Larsell,[8b] fig. 15).

The cerebellar commissure is prominent in the adult frog and connects the two sides of the main cerebellar mass. At the time this study was made the relations between cells of the superior trigeminal nucleus region and the cerebellar commissure were not clear, but some fibers which appeared to pass from the neighboring secondary visceral nucleus, in this crowded region of the frog's brain, to the cerebellar commissure must be regarded in the light of subsequent studies as secondary trigeminal or corpus cerebelli fibers. Direct trigeminal fibers also pass into the cerebellar commissure of the frog, as do spinocerebellar fibers.

The great development of the corpora cerebelli and the relative reduction in size of the vestibular part of the cerebellum of the adult frog have obliterated the sulcus noted on the anterodorsal surface of the cerebellum in Triturus.

REPTILES

In reptiles the cerebellum shows a great variety of forms according to the method of locomotion in the different groups. All are characterized by absence of the lateral-line system, but the vestibular connections are present in varying degrees of development in the different groups. The homolog of the structure designated as the auricular lobe in amphibians will be called the floccular lobe in reptiles and mammals. In the latter groups it receives only vestibular fibers, in contrast to the vestibular and lateral-line connections of amphibians.

The simplest cerebellum in the reptiles appears to be that found in the legless lizard Anniella,[9a] in which the organ consists of a commissural mass of fibers with a thin zone of accompanying granular layer. The commissure is composed of fibers which arise laterally in the region of the corpus cerebelli and superior fifth nucleus (Larsell,[9a] fig. 19). The ventral spinocerebellar tract runs as a distinct bundle dorsal to the cerebellar commissure. A small lateral projection which receives vestibular fibers is present, and is considered a rudimentary floccular lobe. No myelinated fibers were observed connecting the two flocculi, and silver preparations of this lizard were not available for the study of unmyelinated fibers. It appears doubtful whether a lateral commissure is present, but Anniella is unquestionably a degenerate form in which there has been some loss of structure.

Passing by the snakes, lizards and turtles, in which groups there are various degrees of development of the cerebellum and its connections, I shall pay more particular attention to the alligator.[9b] Sagittal sections

9. Larsell, O.: (*a*) The Cerebellum of Reptiles: Lizards and Snake, J. Comp. Neurol. **41**:59, 1926; (*b*) The Cerebellum of Reptiles: Chelonians and Alligator, ibid. **56**:299, 1932.

of Alligator mississippiensis of Reese's stage XIX+ have a furrow on the dorsal surface which the study of subsequent stages shows to mark the boundary between the corpus cerebelli and the floccular lobe. It also bounds the caudomedial continuation of the latter from the corpus cerebelli. In the alligator, as in the turtles, the corpus cerebelli has become massive. The floccular lobe, which receives vestibular fibers only, is much smaller. The corpora cerebelli are connected by an important bundle of fibers constituting the cerebellar commissure. No silver material of the alligator has been available to me, and the fibers do not show up as distinctly as desirable for conclusive results in sections of embryos stained with Lyons blue or in Weigert preparations of the young alligator. A restudy of these series, however, shows a small bundle of fibers along the lateral and caudal margins of the cerebellum which in general corresponds in position to the lateral commissure of amphibians. Whether or not these fibers cross the midplane and thus

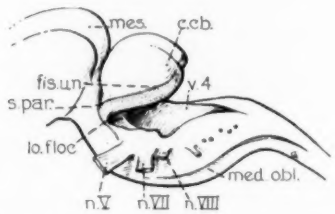


Fig. 6.—The cerebellum and adjacent region of an alligator embryo of Reese's stage XXI + (slightly modified from Larsell, O.: J. Comp. Neurol. **56**:299, 1932); about × 5. The floccular lobe is stippled.

form a commissure could not be determined in the material available. Similar uncertainty resulted from reexamination of embryo and adult turtles, and the presence of a lateral commissure in the reptilian cerebellum must be left in doubt.

The external furrow is more marked in the embryo alligator beginning at about Reese's stage XXI, so that it is visible externally with the naked eye (fig. 6). It extends from above the floccular lobe caudally and medially, as previously described, separating the great swelling of the corpus cerebelli from the flocculus, rostrally, and also separating the corpus cerebelli from the caudomedial continuation of the flocculus. Weigert preparations of the brain of the young alligator show that only vestibular fibers pass into the flocculus and this caudomedial continuation, which corresponds to the nodulus of mammals. On the ground of development, relationship and fiber tract connections, we are justified in grouping the flocculus and the incipient nodulus together as the floccular lobe. The reptilian cerebellum consists, then, of the corpus cerebelli and the floccular lobe, with the parafloccular sulcus, continued

caudomedially as in figure 7, *fis. un.*, as the external boundary between them. Because of the great preponderance of muscle sense impulses over the vestibular impulses in the reptiles, the corpus cerebelli has become the predominant element of the cerebellum. Similar relationships between a ventrally placed floccular lobe and a dorsomedial corpus cerebelli are found in the turtles, especially in the sea-turtle, Chelonia midas, but these forms do not as clearly show the caudomedial continuation of the flocculi as does the alligator. Embryo turtles of various stages, however, do show it and also the external furrow between it and the corpus cerebelli.

A second feature of note in the cerebellum of the alligator is the appearance of two fissures on the surface of the corpus cerebelli. These

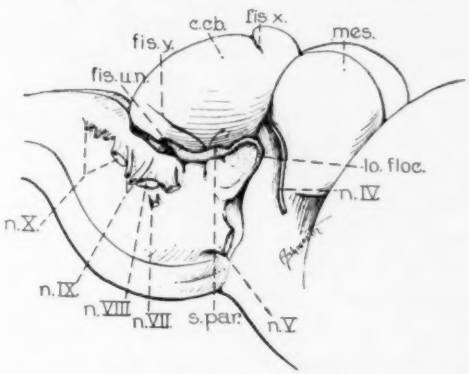


Fig. 7.—The cerebellar region of a young alligator (slightly modified from Larsell, O.: J. Comp. Neurol. **56**:299, 1932); about × 5. The floccular lobe is stippled.

may be seen grossly in the young alligator (fig. 7) and also in sagittal sections, but they are not present in the embryo as late as Reese's stage XXII+, although the fissure *un.* is visible both at this stage and earlier. The fissures in the corpus cerebelli, which, following Ingvar,[10] are labeled *fis. x* and *fis. y*, are evidently the result of further increase in volume of the corpus cerebelli, accompanied by the beginning of folding at right angles to the rostrocaudal axis. This folding results first in fissure *x*, rostrally, which without question is homologous to the fissura prima of Elliott Smith[11] in mammals, and subsequently fissure *y*, which, it appears to me, corresponds to Elliott Smith's fissura secunda rather than to the prepyramidal fissure, as held by Ingvar.[10]

10. Ingvar, S.: Zur Phylo- und Ontogenese des Kleinhirns, Folia Neurobiologica **11**:205, 1918.

11. Smith, G. Elliott: Notes on the Morphology of the Cerebellum, J. Anat. & Physiol. **37**:329, 1903.

The flocculus is closely related, both in position and by its connections, with the vestibular part of the medulla oblongata. It appears to receive only direct vestibular fibers in the reptiles studied. This observation is based on Weigert preparations and lacks the confirmatory evidence of Marchi series, but it is in agreement with the conclusions of Ingvar from mammalian experimental material, and with my own observations in silver series both in amphibians and in small mammals.

Fiber Tracts.—The reptilian cerebellum shows the same fiber tracts in general as that of amphibians, save that the lateral-line systems are completely lacking (fig. 8). The tracts have been described in detail elsewhere,[9] and only the points of difference between reptiles and lower

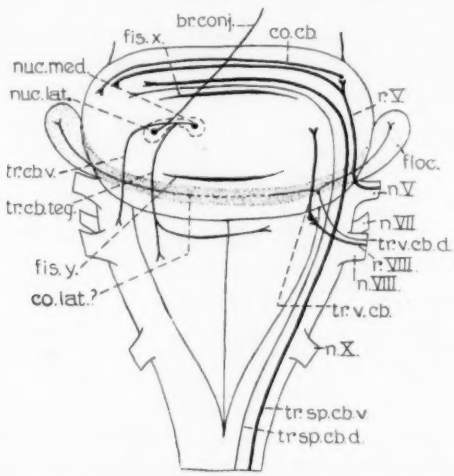


Fig. 8.—Diagram of the cerebellum and its principal fiber tracts in reptiles. The floccular lobe is stippled.

forms need be referred to, together with the fact that there has been demonstrated a definite trigeminal bundle to the cerebellum, and that the cerebellar commissure arises from cells of the superior fifth nucleus region. A dorsal spinocerebellar tract also makes its appearance in reptiles. The fibers are derived in part from the bulb, but also the cord contributes to the bundle. The ventral spinocerebellar tract appears to be the older, distributing to the rostral part of the corpus cerebelli. The dorsal spinocerebellar tract in the alligator sends its fibers chiefly into the caudal part of the corpus cerebelli. The spinocerebellar fibers do not reach the lateral or caudal margins of the cerebellum in the turtles or alligator. This is the region of the floccular lobe. In the alligator, as shown in sagittal sections, there is a zone between the rostral and the caudal parts of the cerebellum into which but few spinocerebellar fibers pass. This and other evidence points to the zone between fissures *x*

and *y* as being in part a new region of the cerebellum superimposed on the previously existing spinocerebellar and vestibular parts. In the reptiles I have been unable to find evidence of pontile fibers, but in mammals such fibers pass into this region, the middle lobe.

As compared with that of urodele amphibians, the reptilian cerebellum stands in contrast by the complete absence of the lateral-line fiber tracts, with consequent reduction or modification of the auricular lobe of amphibians into the flocculus. In lizards and snakes this part of the cerebellar apparatus is quite small, but it becomes more important in chelonians and crocodilians. A second point of striking contrast lies in the great development of the corpus cerebelli in most of the reptiles, as compared with the small corpus cerebelli of amphibians. Advances toward the mammalian type of cerebellum are evident in the sulci which appear in the corpus cerebelli of the alligator, with the resultant division of this part of the cerebellum into three lobes, an anterior, a middle and a posterior lobe. The anterior and middle lobes are identical respectively with the lobus anterior and lobus medius, described by Ingvar. The posterior lobe of the present division does not correspond to that spoken of by Ingvar [10] in reptiles, since he includes the flocculi and the swelling (the incipient nodulus) ventral to the posterior lobe, as heretofore defined. This incipient nodulus has been shown to connect the two flocculi and to constitute with them a morphologically more fundamental division of the cerebellum, namely, the floccular lobe, as defined previously. The three lobes formed by the fissures on the corpus cerebelli are therefore secondary divisions of the trigeminal and spinocerebellar portion of the cerebellum, namely, the corpus cerebelli, while the floccular lobe represents the primary vestibular part of the organ.

The principal points of similarity between the amphibian and the reptilian cerebellum, aside from the more obvious features of cell layers and principal fiber tract connections, consist in the corpora cerebelli in each, connected by the trigeminal commissura cerebelli, and the continuity between the auricular (floccular) lobes. These two primary divisions of the lateral halves of the cerebellum are thus connected to the corresponding parts of the opposite side by a bridge of fibers or of cells or of both cells and fibers.

MAMMALS

The mammalian cerebellum has been described by so many writers with reference to surface anatomy as well as to microscopic structure that no attempt is made here to enter into details. The point of view presented is the morphologic one in an attempt to correlate the large accumulation of data on the organ in mammals with the foregoing interpretation of the cerebellum in lower vertebrates. The conclusions set forth are based on studies of several mammals, including chiefly the

mole (Scapanus townsendi), a small and primitive bat (Myotis) and the opossum (Didelphys), which will be described in detail elsewhere. Through the courtesy of Dr. Jeanette B. Obenchain [12] I have also had an opportunity to examine her series of sections of the primitive marsupials Caenolestes and Orolestes. The material from the moles and bats included several brains cut in serial sections after having been stained with the pyridine-silver technic, in addition to iron-hematoxylin and other series.

For the sake of clearness the cerebellum of the fetal mole will first be described briefly because it resembles most closely that of the alligator. A model reconstructed from serial sagittal sections is illustrated in figure 9. It will be noted that the corpus cerebelli is large and overshadows the flocculus. The latter, however, is continuous caudomedially

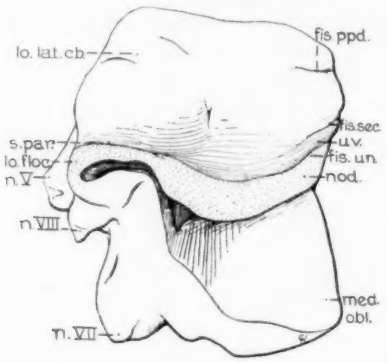


Fig. 9.—The cerebellum of a fetal mole (Scapanus townsendi), drawn from a model; about × 17. The floccular lobe is stippled.

with a ridge separated from the corpus cerebelli by a furrow. Rostrally this furrow continues into the parafloccular sulcus between the flocculus and the corpus cerebelli. Caudomedially it occupies the position of the uvulonodular or postnodular fissure of mammals. I regard it as corresponding to this fissure, and the ridge which lies ventrad to it in the fetus of the mole is certainly the nodulus, which is obviously continuous with the flocculus in the model. The relations are well shown in sagittal sections (fig. 10).

In addition to the uvulonodular fissure this cerebellum shows a definite fissura prima and a fainter fissura secunda. There is also a slight furrow in the position of the prepyramidal fissure, but these markings, with the exception of the fissura prima, extend but a short distance to either side of the midplane at this stage of development. The fissura

12. Obenchain, J. B.: The Brains of the South American Marsupials Caenolestes and Orolestes, Pub. 224, Field Mus. of Nat. Hist. Zoöl. Series **16**:175, 1925.

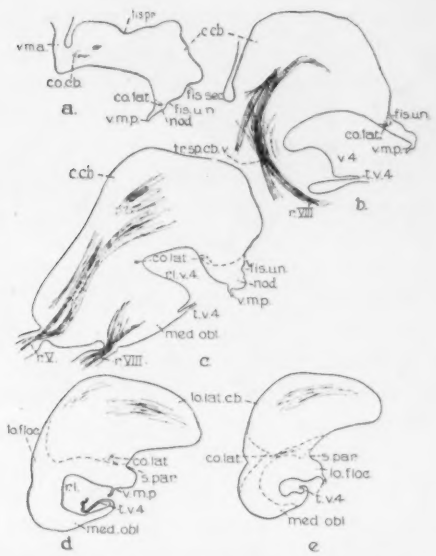


Fig. 10.—Sagittal sections through the cerebellum of a fetal mole (Scapanus townsendi): *a*, midsagittal plane; *b*, *c*, *d* and *e*, sections made successively farther laterad; about × 17.

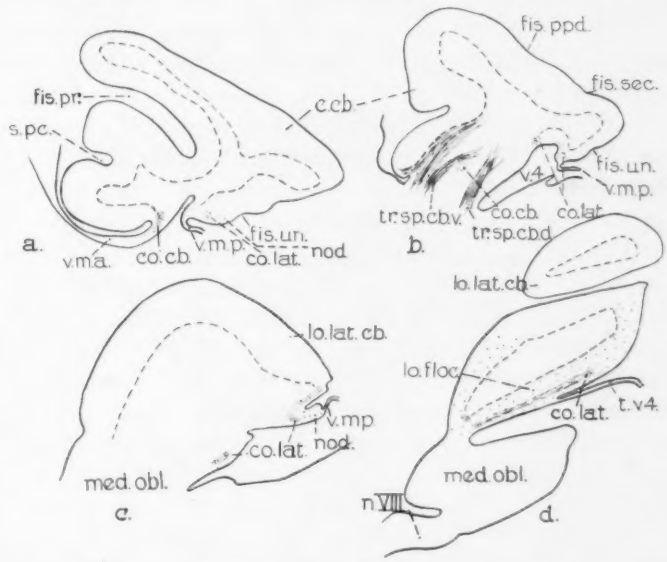


Fig. 11.—Sagittal sections through the cerebellum of a new-born mole (Scapanus townsendi): *a*, midsagittal plane; *b*, *c* and *d*, sections made successively farther laterad; × 25. The parts related to the floccular lobe are stippled.

prima extends farther laterally, but not into the lateral lobe of the cerebellum. These are all fissures on the surface of the corpus cerebelli, deeper than in the young alligator and with an additional one, the prepyramidal sulcus, but recalling the cerebellum of this reptile.

At this stage of development of the mole fetus the fibers in the cerebellum are still distinguishable as definite bundles. As illustrated in figure 10, there is a distinct commissura cerebelli, and direct trigeminal fibers enter into the more ventral part of the corpus cerebelli. A small bundle of fibers also continues into the floccular region from the vestibular nerve, to run parallel with the parafloccular fissure and its continuation, the uvulonodular sulcus. This is the lateral commissure passing from the vestibular root and the flocculus of one side to the corresponding regions on the opposite side of the cerebellum.

In the new-born mole the corpus cerebelli has greatly increased in size and has extended laterally as the lateral cerebellar lobes. The fissura prima is much deepened, but the fissura secunda remains relatively shallow (fig. 11). This appears to be due to the marked forward folding of the nodulus. A new fissure has appeared in the anterior lobe which corresponds in position to the sulcus postcentralis.

The parafloccular sulcus and its caudomedial continuation, the uvulonodular fissure, are present. The flocculus has increased considerably in size as compared with the fetal stage described, as has also the nodulus in the region corresponding to the vermis. Between the flocculus and this midregion, however, the floccular lobe has become attenuated so that there is but a narrow band of molecular layer connecting flocculus and nodulus. Parallel to this, however, the lateral commissure has its course from the flocculus caudomedially. At least some of its fibers are direct vestibular fibers.

Myotis.—In the small bat, Myotis, the cerebellum is very simple, although it shows the characteristic mammalian features. The fissures described in the fetus and new-born of the mole are the only ones present in the adult bat, but these are greatly deepened by the growth and folding of the cerebellar cortex on either side of them. They are best seen in sagittal sections (fig. 12). The fiber tracts which enter the cerebellum of this bat are distinct enough to be followed for some distance, particularly in silver preparations. A definite cerebellar commissure is recognizable near the base of the main part of the organ (fig. 12 *co. cb.*) in the region corresponding to the position of this commissure in reptiles. The source of the fibers is not clear, but the commissure is sufficiently distinct from the accompanying ventral spinocerebellar tract to indicate a separate origin in the rostral region of the medulla oblongata and base of the cerebellum. They intermingle with fibers of the spinocerebellar and secondary vestibular tracts and are

apparently distributed with these fibers to the various folds of the cerebellum except for the floccular lobe. This is in agreement with the recent conclusions of Jansen [13] based on experimental lesions in the cerebellar cortex of the rabbit, followed by Marchi staining. He found evidence of a cerebellar commissure connecting the hemispheres, but concluded that there is "no associational connection between the cortex of the floccular formation and the cortex of either hemisphere or vermis."

The flocculus of Myotis is small, in contrast to the large paraflocculus found in this species. The latter will be touched on but briefly, pending further study as to its morphologic relationships and development, but the flocculus clearly has the same relationships in the adult bat as

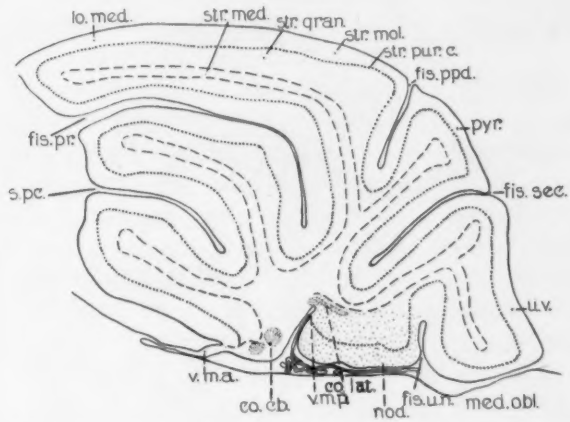


Fig. 12.—Midsagittal section through the cerebellum of an adult bat (Myotis); about × 25. The nodulus is stippled.

have been described in the fetus and new-born of the mole and also in the alligator. In the bat it has been pushed farther laterally by the widening of the cerebellum, but it retains its intimate connections with the vestibular region of the medulla oblongata, and also its connections with the nodulus of an attenuated continuation of cortical substance, as well as by a distinct band of fibers which occupy the same relative position and have the same relationships as the lateral commissure in the mole. This band of fibers crosses the midplane (fig. 13), and laterally, where the cerebellum joins the medulla oblongata, the fiber bundle can also be followed into the latter. In transverse series it is clear that some of the fibers pass directly from the bulb to the flocculus of the same side. The majority, however, turn medially to continue to the contralateral

13. Jansen, Jan: Experimental Studies on the Intrinsic Fibers of the Cerebellum: I. The Arcuate Fibers, J. Comp. Neurol. **57**:369, 1933.

flocculus, and it is these fibers coming from the two sides of the floccular lobe which form the commissure in the nodular region and which continue laterally through the attenuated part of the nodulus to the flocculus on either side.

Ingvar [10] has shown by the Marchi method that in the cat no spinocerebellar fibers reach the nodulus or flocculus, while both spinocerebellar and vestibular fibers reach the remaining parts of his "first story" of the cerebellum, namely, the uvula and lingula. This statement is substantiated in the bat and also in the mole series. The floccular lobe (auricular lobe of lower forms) is accordingly distinctive throughout the vertebrates studied, from the amphibians to the mammals, in

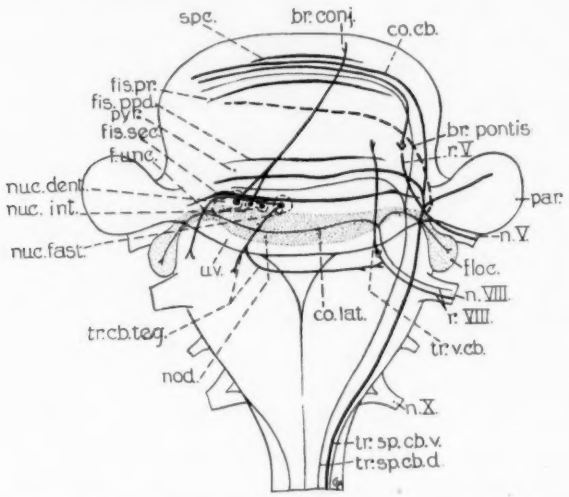


Fig. 13.—Diagram of the cerebellum and its chief fiber tracts in the bat (Myotis). The floccular lobe is stippled.

being vestibulolateral or purely vestibular, while the corpus cerebelli is primarily spinocerebellar and trigeminal, that is, primarily concerned with muscle sense. The lateral or vestibular commissure demonstrated in the mammals, as in lower forms, adds to the evidence which indicates that the floccular lobe is morphologically of equal rank with the corpus cerebelli and should not be regarded merely as a part of the lobus posterior of Ingvar, bounded anteriorly by the prepyramidal fissure, or even the posterior lobe of Elliott Smith,[11] bounded by his fissura secunda. On the basis here presented there would remain only the uvula and paraflocculus in the posterior lobe of Elliott Smith, after the nodulus and flocculus are segregated as the floccular lobe. Of Ingvar's lobus posterior there would remain the pyramis, uvula and paraflocculus. It should be noted that the floccular lobe as here defined excludes the paraflocculus.

Riley's [14] studies of the cerebellar gyri in a large number of mammals indicate that the flocculus and the paraflocculus are distinct structures. This is also shown by Ingvar's [10] studies on the human fetus. Ingvar is in agreement with Elliott Smith [11] and Bradley [15] that the paraflocculus joins with the uvula and pyramis, while the flocculus is joined to the nodulus. My own studies on the simple cerebellum of the mole and of the bat confirm this. It appears to me that the connections between the uvula and nodulus across the uvulonodular fissure, shown by Elliott Smith in the adults of many mammals, are secondary. Certainly in the embryos of all mammals (including man) in which the uvulonodular fissure has been described, it is continuous from side to side and is described as the first to appear or, by some authors, as appearing at about the same time as the fissura prima. The more closely graded the embryos on which such studies have been made, however, the greater is the tendency on the part of authors to designate the uvulonodular fissure as the first to appear.

The lingula and the uvula, according to Ingvar,[10] receive both direct vestibular and spinocerebellar fibers in the cat. The lobulus simplex and the paraflocculus, on the other hand, receive no direct vestibular fibers, but in common with most parts of the cerebellum they receive spinocerebellar and secondary vestibular fibers. The bat shows clearly that pontile fibers enter the medial lobe, primarily. Jansen's [18] recent work has demonstrated that different parts of the cerebellum are interconnected by association fibers. Adopting Ingvar's excellent figure of the cerebellum as a building composed of several stories, the present analysis would consider the vestibular floccular lobe, with its flocculus and nodulus, as the foundation and basement of the building. The corpus cerebelli, representing the superstructure, would be divided, in mammals, into lingula and uvula, with both direct vestibular and spinocerebellar connections as the first story; the culmen, pyramis, paraflocculus and lobulus simplex, with spinocerebellar connections, as the second story; and the newer lobus medius, with pontile connections chiefly, as the third story.

CEREBELLAR NUCLEI AND EFFERENT TRACTS

In larval Amblystoma a group of cells, which is continuous ventrally with the general tegmentum of the bulb and dorsally with the corpus cerebelli, is found which, as sections stained by Golgi's method show, sends groups of axons in various directions. One group of fibers, forming a loose bundle, passes medially, running roughly parallel with the

14. Riley, H. A.: The Cerebellum, Association for Research in Nervous and Mental Diseases, Baltimore, Williams & Wilkins Company, 1929, p. 37.

15. Bradley, O. Charnock: On the Development and Homology of the Mammalian Cerebellar Fissures, J. Anat. & Physiol. **37**:112, 221, 1903.

cerebellar commissure for the greater part of its course, crossing to the opposite side and then turning caudally as the crossed cerebellotegmental tract. A similar tract (fig. 4) is well shown in adult Triturus.[7] In the frog,[8] larval and adult, there is a cerebellotegmental tract which is not so clearly crossed. It is probable that both crossed and uncrossed fibers are present.

Other fibers from the same group of cells are directed rostrally into the tegmentum of the midbrain, and represent the incipient brachium conjunctivum. Still other axons pass into the medulla oblongata as arcuate fibers; indeed, in early stages of Amblystoma [5] the cerebellotegmental fibers as well as the group designated as brachium conjunctivum, have the aspect of an elongated bundle of arcuate fibers.

In the adult salamander and especially in the adult frog the cell group which gives rise to these cerebellar efferent fibers is distinct enough to merit the designation nucleus cerebelli.[8b] It is still continuous ventrally with the bulbar tegmentum but projects upward into the corpus cerebelli. In the developing and young frog the foreshortened condition of this part of the brain stem makes the nucleus cerebelli appear continuous with the vestibular nucleus (Larsell,[8b] fig. 18), but the former is distinguishable by its larger cells and the direction of its axons. Perhaps some of the cells should be regarded as vestibular.

Reptiles show a differentiation into two masses of cells, a medial nucleus and a lateral cerebellar nucleus, with a narrow bridge of cells connecting them (fig. 8), as shown in greater detail in figures 19 and 21 and figures 15 to 17, respectively, of my articles on the reptilian cerebellum.[9] Sections of the cerebellum of the turtle stained by Golgi's method show axons from the medial nucleus passing medially, apparently forming an incipient fasciculus uncinatus, while the lateral nucleus sends its axons into the midbrain as the brachium conjunctivum. Sections of the cerebellum of the alligator stained by Weigert's method confirm this general arrangement.

In the bat, Myotis, the deep cerebellar nuclei consist of a medial group of rather large cells which have vestibular connections, an intermediate group and a lateral group of cells. The medial group is without question the fastigial nucleus (fig. 13). Lateral to it, and to a considerable degree separated from it by fibers, the intermediate group of cells consists chiefly of smaller cells, with some large ones, and is roughly divided into two parts. This is regarded as the nucleus interpositus or intermedius of Weidenreich,[16] Brunner [17] and Allen.[18] The last-men-

16. Weidenreich, F.: Zur Anatomie der zentralen Kleinhirnkerne der Säuger, Ztschr. f. Morphol. u. Antrop. **1**:259, 1899.

17. Brunner, H.: Die zentralen Kleinhirnkerne bei den Säugetieren, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **22**:200, 1919.

18. Allen, W. F.: Distribution of Fibers Originating from the Different Basal Cerebellar Nuclei, J. Comp. Neurol. **36**:399, 1924.

tioned author and others have stated that the medial part of the nucleus intermedius, corresponding to the nucleus globosus of higher mammals, contributes fibers to the brachium conjunctivum. Allen's studies led him to conclude that there are two functional nuclei in mammals: a lateral one including the dentate, emboliform and globose nuclei, the emboliformis and globosus together forming the nucleus intermedius, and the medially placed nucleus fastigii or tecti. The lateral group, according to Allen, gives rise to the brachium conjunctivum and has its afferent supply chiefly from the cortex of the cerebellar hemispheres. The medial or fastigial nucleus gives rise to most of the cerebellobulbar fibers, including the fasciculus uncinatus of Russell. Mussen [19] and Rasmussen [20] concluded that the globose nucleus, in cats and monkeys, together with the fastigial nucleus, forms a medial nucleus with vestibular connections, while the emboliform and dentate nuclei may be considered as a lateral mass of cells giving rise to the brachium conjunctivum. In the bat there are three distinct groups of cells, with the middle group showing a partial separation into two secondary masses. Of the three primary groups the lateral one is without question the nucleus dentatus. Connected with it by a string of cells is a more laterally placed secondary mass of cells which corresponds to the so-called pars floccularis of the nucleus dentatus, described in many mammals. The name pars paraflocculari s would appear more appropriate, so far as the material from the bat shows.

The silver and iron-hematoxylin series of the brains of bats are not adequate to settle these conflicting views based on Marchi preparations of brains in which the various deep cerebellar nuclei had been destroyed. It can be said only that the lateral nuclear mass obviously gives rise to the brachium conjunctivum, and the medial, rather circumscribed fastigial nucleus just as obviously gives rise to the fastigiobulbar fibers. The intermediate nuclear mass contributes also to the brachium conjunctivum, but whether the more medial portion of it, corresponding to the nucleus globosus, sends its fibers to the brachium conjunctivum or to the vestibular nuclei could not be determined.

In the vertebrate series there is a gradual differentiation of deep cerebellar nuclei from a single mass of cells connected with the tegmentum in amphibians (figs. 4 and 5), through the stage of two nuclei (fig. 8), medial and lateral, in reptiles, to medial, intermediate and lateral nuclei (fig. 13) in lower mammals and to a final differentiation into the four nuclei characteristic of the higher mammals and of man.

19. Mussen, A. T.: The Cerebellum, Association for Research in Nervous and Mental Diseases, Baltimore, Williams & Wilkins Company, 1929, p. 381.

20. Rasmussen, A. T.: Origin and Course of the Fasciculus Uncinatus (Russell) in the Cat with Observations on the Other Fiber Tracts Arising from the Cerebellar Nuclei, J. Comp. Neurol. **57**:165, 1933.

In the lamprey van Hoëvell [21] found a group of cells, which he called the anterior octavomotor nucleus, sending fibers into the midbrain which have many points of similarity to the brachium conjunctivum. Van Hoëvell and also Ariëns Kappers [22] regarded this nucleus as homologous to the anterior part of the vestibular nuclear mass of higher forms. It would take me too far afield to discuss the homologies of this region in detail, and it must suffice for the present merely to point to the fact that in Petromyzon, in which spinal connections with the cerebellum are doubtful, and in which the vestibular connections are certainly predominant together with a small trigeminal root (Tretjakoff [23]), the efferent cerebellar nucleus is closely related to the vestibular nuclei. In the amphibians, in which spinocerebellar connections are present, the nucleus cerebelli, while still a single mass, extends more obviously into the cerebellar structure, although retaining its connection with the tegmentum and its close relationship to the vestibular nucleus, as shown in the frog. In the reptiles there begins the segregation of cells into the two principal functional groups, namely, the medial group whose connections are primarily vestibular and the lateral group whose connections are with the midbrain and the tegmentum. The anterior octavomotor fibers of Petromyzon, described by van Hoëvell [21] as passing into the midbrain and decussating there much like the brachium conjunctivum of higher forms, require further study. In the light of the conflicting results of various experimental workers on mammals with reference to brachium conjunctivum fibers from the region of the globose nucleus, strict homologies between the lowest and the highest vertebrates with reference to these nuclei must be avoided for the present. The differentiation from the general nucleus cerebelli of amphibians to the four deep nuclei of mammals, however, appears to proceed by stages that are easy to follow. The vestibular part is certainly the oldest, phylogenetically, and the nucleus dentatus the most recently differentiated. This sequence has also been found by Dowd [24] in the ontogenetic development of these nuclei in the pig.

The intimate connections demonstrated by Allen [18] and others between the fastigial nucleus and the vestibular regions of the cerebellum and bulb and the recognized relations between the dentate nucleus and the newer part of the cerebellar cortex, with its pontile connections,

21. van Hoëvell, J. L. D.: The Phylogenetic Development of the Cerebellar Nuclei, Proc. Kon. Akad. van Wetenschappen te Amsterdam **18**:1421, 1916.

22. Ariëns Kappers, C. U.: Die vergleichende Anatomie des Nervensystems, Haarlem, De Erven F. Bohn, 1920-1921.

23. Tretjakoff, D.: Das Nervensystem von Ammocoetes: II. Das Gehirn, Arch. f. mikr. Anat. **74**:636, 1909.

24. Dowd, L. W.: The Development of the Dentate Nucleus in the Pig, J. Comp. Neurol. **48**:471, 1929.

suggest that the globose and emboliform nuclei may have relations to the first and second cerebellar "stories" similar to those which the fastigial and dentate nuclei, respectively, have to the basal and the most recently acquired cerebellar parts. Such a relation to the lingula and uvula and to the culmen and pyramis and their related cerebellar parts would be difficult to demonstrate experimentally, and must remain for the present as a suggestion supported only by the morphologic fact that the other cerebellar nuclei are differentiated in the order represented by the formation of the successive cerebellar stories. Since these nuclei receive their afferent impulses chiefly from the Purkinje cells of the cerebellar cortex it appears plausible that the successive separation of the various nuclear masses as new regions of cerebellar cortex are differentiated, in the process of evolution of the organ, is in response to Kappers' law of neurobiotaxis.

Clinical Notes

ACUTE POLIOMYELITIS WITH CHOKED DISKS

Notes on Prolonged Observation of the Spinal Fluid and the Use of the Respirator

J. B. Ayer, M.D., and L. D. Trevett, M.D., Boston

The publication of a report of an individual case of acute poliomyelitis requires justification. Our decision to put this case on record is based on the following reasons: First, we believe that the patient's life was saved by the use of the respirator. Second, persistent increased intracranial pressure was present, accompanied by choked disk. Third, long-continued observation was made of the spinal fluid. Fourth, we believe that the patient suffered a relapse during the acute stage of the disease.

REPORT OF CASE

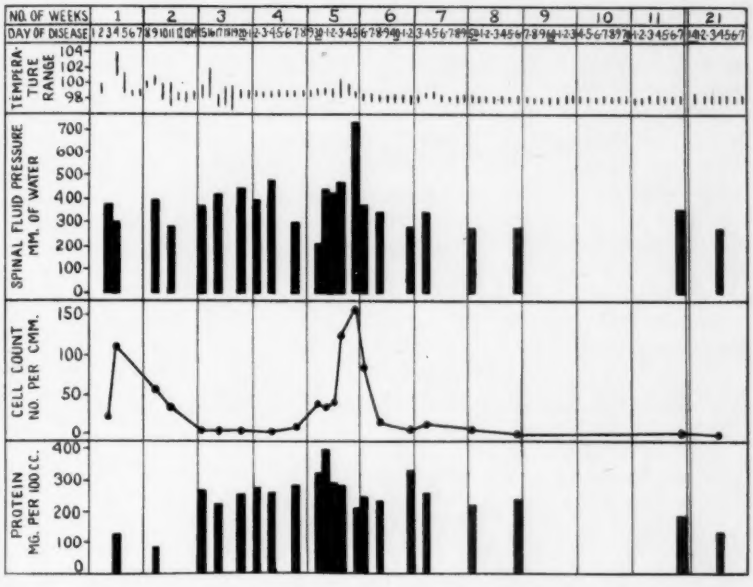
A youth, aged 17, with an unimportant medical history, was first taken ill on Aug. 4, 1932. Malaise, lasting less than twenty-four hours, was followed by apparent recovery until August 10, when he complained of chilliness, fever, headache and backache. Lumbar puncture at that time, more than forty-eight hours before the onset of the paralysis, showed twenty mononuclear cells per cubic millimeter, with a trace of globulin and positive sugar reduction. Early on August 13, nine days after the first symptom and three days after the second, if one admits this to be of the "dromedary type," paralysis set in. The initial weakness was observed in the left iliopsoas muscle, but by the afternoon of the same day the the patient exhibited a weakness of the left quadriceps, rotators and adductors of the left thigh, a weakness of the abdominal muscles, and the absence of visible or measurable expansion of the chest. Flexion of the neck on the chest was weak, and catheterization was necessary. The cranial nerves were normal. Because of the presence of intercostal paralysis, the patient was brought to Boston to be near a respirator, if its use were necessary. The trip of 200 miles by aeroplane, flying at low altitude, was accomplished with a minimum of discomfort and no increase in dyspnea.

On the next day, August 14, a more extensive paralysis was apparent; the right deltoid muscle, both triceps muscles and the muscles of the right lower extremity being affected. A transitory nasal voice and slowness in deglutition alone suggested involvement of the medulla. The optic disks were slightly blurred. Hyperesthesia was, of course, marked. During the first three weeks of the illness the case ran the usual course of acute poliomyelitis of the extensive and severe type. The respirator was in use for from fourteen to eighteen hours a day, and although no cessation of respiration occurred requiring immediate relief, periods of gradual increase in cyanosis and dyspnea, restlessness and apprehension on the part of the patient gave warning that artificial respiration was becoming necessary. At those times, the use of the respirator would always lead to immediate relief and usually to sleep.

By the end of the third week, motor function had definitely improved, although no chest expansion was seen, and the temperature and the cell count in the fluid

had fallen to normal. It seemed reasonable to assume that the patient was convalescent. But on September 12, early in the fifth week of the paralysis a rise in temperature, an increase in tenderness and hyperesthesia, an attack of vomiting and a marked rise in the cells in the spinal fluid ushered in a period of several days of anxiety to all concerned, which it was soon felt must represent a relapse or recrudescence of the pathologic process. Severe headache, increase in fluid pressure to 700 mm. and an increasing papilledema formed a group of findings which at this time seemed quite out of keeping with a diagnosis of poliomyelitis, but which we now consider as a complication of unusual character.

Following this relapse, which lasted the better part of a week, and during which the papilledema measured up to 2 diopters in each eye, convalescence



Shows persistence of high spinal fluid pressure and protein over a period of five months. Relapse is indicated in the fifth week of the disease.

again set in and continued thereafter uninterruptedly. Persistence of high fluid pressure and protein and very slow subsidence of the papilledema during a long period are noteworthy and will be discussed. During the whole period of five months while the patient was under our care the respirator was used. Even when not strictly necessary it was found to be of great benefit in resting the patient or in conserving his energy.

THE USE OF THE RESPIRATOR

Since its introduction by Drinker and McKhann[1] in 1929, the use of this instrument has become so widespread as to require little comment here.

1. Drinker, P., and McKhann, C. F.: The Use of a New Apparatus for Prolonged Administration of Artificial Respiration, J. A. M. A. **92**:1658 (May 18) 1929.

Wilson,[2] Crone [3] and many others have adequately treated and discussed its use and advantages. Our experience and that of others has been that its use is particularly beneficial to patients with intercostal and diaphragmatic paralysis. The present case falls into that group. Wilson emphasized the fact that "the respirator should be looked upon as more than an instrument simply to prevent death from asphyxiation." Legg [4] agreed with this point of view. In the case under discussion the respirator is still being used, eight months after the onset of the disease, in spite of the fact that for a long time its use has not been strictly necessary. Passive exercise is considered good treatment for peripheral palsies; and the respirator is an ideal instrument for providing passive movement to the intercostals and the diaphragm. When he was first seen, the patient's chest expansion was nil; after five months it was 5 cm., and measurement of vital capacity was proportionate. A rapid pulse rate was markedly reduced when the respirator was employed.

In the early stage of the illness restlessness was excessive and medication with hypnotics was necessary; it was found that the use of the respirator at this time greatly minimized the necessity for such drugs.

In this case, therefore, we feel certain that the patient's life, in the acute stage, was saved by the use of the respirator and that in the convalescent period the instrument provided beneficial periods of rest and passive exercise.

CHOKED DISK

The patient showed early a very slight blurring of the edges of the disks with engorged veins. It was not, however, until the fifth week of the illness, during the relapse, that papilledema developed to a measurable quantity. At this time the edges of the disks were lost to view, the disks themselves were pink and protruded about 2 diopters, and in one eye small retinal hemorrhages appeared close to the disk but not on it. At no time were the maculae thought to be abnormal, and at no time was exudate seen. The vision was unaltered, so far as it could be tested with the patient in bed and without instruments of precision. The papilledema subsided very slowly; over two months later the disks were still found to be abnormal by Dr. E. T. Easton, who stated: "Both optic disks still show marked blurring of outline and it is likely to be a long time before that changes much, with the probability that the disk outline may not become normally sharp. The vision, so far as I could determine by the test possible, is up to full normal standard. Maddox rods test indicated a normal muscle balance."

There may well be a difference of opinion as to whether the changes in the fundus were due to increased intracranial pressure or represent severe optic neuritis from inflammation. We lean toward accepting the former explanation because of the appearance described, because of the retention of excellent sight, even when the disks were most choked, and because of the presence of long-continued intracranial hypertension, as indicated by repeated examination of the spinal fluid.

The literature is not consistent in the reports on the frequency of papilledema in poliomyelitis. Koplik,[5] in 1916, in discussing the meningitic type of poliomye-

2. Wilson, J. L.: New England J. Med. **206**:887 (April 28) 1932.

3. Crone, N. L.: To be published.

4. Legg, A. T.: The Use of the Drinker Respirator in After-Care of Infantile Paralysis, J. A. M. A. **100**:647 (March 4) 1933.

5. Koplik, H.: Arch. Pediat. **33**:575 (Aug.) 1916.

litis stated that optic neuritis occurs in cases in which increased intracranial pressure persists for some time after the temperature becomes normal. He had also seen hemorrhages in the retina, which, he said, is not uncommon in this type of the disease. Batten,[6] in 1916, said that optic neuritis can occur in the acute stage. Ghormley [7] reported a single case. On the other hand, two large series reported from New York and Pennsylvania failed to show any case with changes in the eyes. Peabody, Draper and Dochez [8] summarized the literature as follows: "The eyegrounds were examined in many of our cases, but we found no abnormalities of the optic nerve. While Wickman has reported one case of optic neuritis in an acute case, and Tedeschi found complete blindness and optic atrophy of the left eye in a chronic case, Müller failed to find any evidence of optic neuritis or choked disk in a large number of acute cases, and he believes that if either is found, the case is almost certainly not one of poliomyelitis." Weisenburg,[9] in an analysis of 717 cases in the Philadelphia epidemic of 1916, found optic neuritis or atrophy in none. It is therefore fair to presume that changes in the disks and retina of the nature recorded here are rare.

RELAPSE IN ACUTE POLIOMYELITIS

It may be thought that we have insufficient grounds for believing that our patient underwent a relapse or recrudescence of the pathologic process. No increase in paralysis was surely noted (although the nurse thought there was a diminution of movement of the toes), but it must be emphasized that paralysis was already so extensive that further weakness might easily have passed unnoticed. Yet the elevation of temperature, the increase in sensitiveness and especially the marked change in the spinal fluid appear to us to be sufficient grounds for considering the change in the fifth week to have been relapse. We are supported in our thesis by the following quotation from James Collier: [10] "Now whatever the books may tell you about dreadful results in a relapse, I have never seen any harm occur, no occurrence of paralysis, and no increase of paralysis."

The literature concerning relapse is rather scanty, but it establishes the fact that relapse may and does occur and, contrary to Collier's dictum, may show marked increase in paralysis. Auerbach,[11] in 1899, reported a case in which an attack in June, 1898, caused a paralysis of the left arm and left leg. Two months later, paralysis of the right leg occurred following another attack. Lovegren,[12] in 1905, reported a case in which paralysis of the left leg was followed in two weeks by partial paralysis of the right arm. Neurath,[13] in 1905, published an interesting case in which three separate exacerbations apparently occurred. A child, aged 5, had a febrile attack associated with weakness of the

6. Batten, F. E.: Acute Poliomyelitis, Lumleian Lectures, Lancet **1**:809 (April 15) 1916.

7. Ghormley, R. K.: Optic Neuritis in Infantile Paralysis, J. A. M. A. **84**: 570 (Feb. 21) 1925.

8. Peabody, F. W.; Draper, G., and Dochez, A. R.: A Clinical Study of Acute Poliomyelitis, New York, Rockefeller Institute for Medical Research, 1912, Monograph no. 4, p. 65.

9. Weisenburg, T. H.: Poliomyelitis, Tr. Am. Neurol. A., 1917, p. 162.

10. Collier, J.: Lancet **1**:321 (Feb. 12) 1927.

11. Auerbach: Jahrb. f. Kinderh. **50**:41, 1899.

12. Lovegren: Jahrb. f. Kinderh. **61**:269, 1905.

13. Neurath: Arb. a. d. neurol. Inst. a. d. Wien. Univ. **12**:297, 1905.

legs in August, with complete recovery. Three weeks later there was an exactly similar attack. Five weeks later there was another attack, which rapidly progressed to complete paralysis and death. The findings at autopsy were considered typical of poliomyelitis. Miller,[14] in 1907, reported a remarkable case in a boy, aged 3½. The onset of the illness occurred on September 14, and by September 17 there was extensive paralysis of the neck, legs and oculomotor nerves. On September 27, he had a relapse with sudden paralysis of the intercostal and rectus abdominis muscles. On October 1, there was sudden paralysis of the muscles of the left shoulder. On October 17, nystagmus appeared and lasted for twelve days. Following the last relapse he improved rapidly, but he died later of bronchopneumonia. Necropsy material, studied by Gordon Holmes, showed changes characteristic of poliomyelitis. It was possible to detect pathologically the age of the lesions in the different parts of the nervous system. Sinkler,[15] in 1908, reported a case in which the right leg was involved, with good recovery. After three weeks, the left leg was involved and became flaccidly paralyzed. Müller,[16] in 1910, stated that he had seen instances of relapse, but gave no detailed case histories. Hennelly,[17] in a publication of the Massachusetts State Board of Health in 1911, reported a case of relapse after about a month. Few details are given. Wickman [18] merely stated that relapses can occur. Romer [19] described a relapse in a monkey on which he was experimenting. The animal was inoculated intracerebrally on Dec. 8, 1909. On December 21 and 22, marked diffuse paralysis occurred. During the next two weeks there was slow but continuous improvement, but on January 9 there was a rapid extension of the paralysis, leading to the death of the animal.

A distinction should undoubtedly be made between relapse occurring during the acute or early convalescent period with which we are concerned and recurrent infection which has also been observed, as in the cases reported by Taylor [20] and by Francis and Moncreiff.[21]

PERSISTENCE OF HIGH SPINAL FLUID PRESSURE AND PROTEIN

Because of persistent headache, always relieved by the withdrawal of spinal fluid, we were given a rare opportunity to follow changes in the fluid during five months. It was a great surprise to us that both pressure and protein remained elevated throughout this period, although the cells had long since dropped to normal (except for the period we term a relapse). We find no reference to analyses of the fluid over such a long period, nor have we observed the changes in the fluid in other cases for such long periods.

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14. Miller: Brain **30**:117, 1907.

15. Sinkler, W., and Starr, M. A.: Epidemic Infantile Paralysis, J. A. M. A. **51**:112 (July 11) 1908.

16. Müller, E.: Die spinale Kinderlähmung, Berlin, Julius Springer, 1910.

17. Hennelly, T. P.: An Investigation Concerning Infantile Paralysis as It Occurred in the City of Fall River in 1910, Bull. State Board of Health, Massachusetts **6**:204, 1911.

18. Wickman: Die akute Poliomyelitis, in Lewandowsky, M., Handbuch der Neurologie, Berlin, Julius Springer, 1911, vol. 2, p. 807

19. Romer, P. H.: Epidemic Infantile Paralysis, translated by H. R. Prentice, New York, William Wood and Company, 1913.

20. Taylor, E. W.: J. Nerv. & Ment. Dis. **44**:207 (Sept.) 1916.

21. Francis, F. D., and Moncreiff, W. F.: J. Nerv. & Ment. Dis. **49**:273 (April) 1919.

The persistence of high pressure and a large amount of protein for many weeks has been observed by a number of writers. Müller, in 1910, noted an almost constantly increased pressure, even several weeks after the beginning of the illness. Wickman, in 1911, constantly found a high pressure in the spinal fluid, even after several weeks. Peabody, Draper and Dochez, in 1912, found that the globulin, which was usually low in the first part of the disease, tended to rise in the second and third weeks and then gradually to fall again. In eleven cases the fluids were analyzed until both cell count and globulin reaction became normal. The return to normal occurred in the third week in two cases; in the fourth, in two cases; in the fifth, in one case; in the sixth, in two cases; in the seventh, in three cases, and in the tenth week in one case. Most of the patients of their series consisted of crying children, and the readings of spinal fluid pressure were therefore unsatisfatory. In the monograph of the New York City Department of Health,[22] published in 1917, a large series of spinal fluids was reported on. Of fifty fluids examined in the eighth week of the disease, all but eleven showed an abnormal increase in protein. Larkin and Cornwall,[23] in 1918, found that increase in pressure is a constant finding. "Our observations lead us to believe that the increase in pressure is the most persistent of the changes in the spinal fluid, and that it does not disappear until several months after the acute symptoms have subsided." They also found that the globulin gradually becomes less and less after the third week. Their figures are recorded only up to the fifteenth day. Regan,[24] in 1918, wrote an article on "The Hydrocephalus of Poliomyelitis." He divided the condition into two types; (*a*) the hydrocephalus of the onset, and (*b*) the hydrocephalus persisting after the first week of the disease. The former he considered practically constant, and to be greatly relieved by lumbar puncture. He found persistent hydrocephalus commonly; in some cases it was so severe as to lead eventually to emaciation and death. The latter cases were rare, and he considered them similar to the few cases of meningococcic meningitis which progress to chronic elevation in pressure leading eventually to death. Greenfield and Carmichael[25] stated: " . . . there is an increase in the quantity of protein, which may rise to 100, 200 or even 300 mg. per 100 cc. of fluid. According to Fraser, this increase is continued to the second or third week, after which there is a decline. But in some cases the protein in excess persists for long periods. Our own experience, which is limited to 20 cases examined in the first 3 months of the disease, shows that as late as the eighth, ninth and even the thirteenth week, there may still be considerable protein excess, in fact, our highest readings, 200 and 300 mg., were obtained 7 and 8 weeks after the onset of the paralysis. In other cases examined at this time the protein was much lower. . . ."

Numerous observers report the persistence of high pressure and a high figure for protein in the fluid; but evidence is lacking that such findings are frequent.

The other fluid constituents in our case are not without interest, especially the cell count, to which reference has been made in connection with the relapse. The sugar content of the fluid in acute poliomyelitis has, in our experience,

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22. Monograph on the Epidemic of Poliomyelitis (Infantile Paralysis) in New York City in 1916, New York City Department of Health, 1917.

23. Larkin, J. H., and Cornwall, L. H.: Arch. Pediat. **35**:459 (Aug.) 1918.

24. Regan, J. C.: The Hydrocephalus of Poliomyelitis, Am. J. Dis. Child. **15**: 259 (April) 1918.

25. Greenfield, J. G., and Carmichael, E. A.: The Cerebro-Spinal Fluid in Clinical Diagnosis, New York, The Macmillan Company, 1925.

invariably been normal. It was with considerable anxiety that a titer of 52.5 mg. per hundred cubic centimeters was obtained at the time of the relapse. The absence of organisms in film and culture and the subsequent clinical course of the illness appear to negative the possibility of an intercurrent bacterial meningitis.

The Wassermann reaction was negative and the colloidal gold test in this case inconsequential.

SUMMARY AND CONCLUSIONS

It is our belief that the life of a patient with extensive paralysis from acute poliomyelitis was saved by the use of the respirator. The respirator was hardly less valuable during the convalescent period in conserving energy, automatically expanding the chest and aiding in sleep. Even after five months, although strictly unnecessary, it was found to be useful in resting the muscles of the chest and in inducing sleep.

The persistence of headache, the occurrence of bilateral choked disk in the fourth week and the maintenance of high spinal fluid pressure over the total period of observation of five months indicate a prolonged period of increased intracranial pressure, unusual in poliomyelitis. The frequent use of lumbar puncture as a successful therapeutic agent in combating these symptoms is stressed.

Perhaps the most interesting feature of the case is the behavior of the spinal fluid, examinations of which were made over a period of five months. The drop in cell count in the third week must be considered normal, but the persistence of a large amount of protein and high pressure of the spinal fluid even after five months is striking and probably unusual (although data of this stage of the disease are almost entirely lacking in our own cases or in the literature). The rise in cell count, pressure of the spinal fluid and amount of protein in the fifth week are, we believe, also unusual, and when correlated with the clinical change at that time (rise in temperature and increase in body hypersensitiveness) in our opinion signify a relapse or recrudescence in the pathologic process.

SPECIAL ARTICLE

THE PRACTICE OF PSYCHIATRY

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Perhaps unwisely, I have accepted a mandate to discuss "The Practice of Psychiatry." The mandate includes an attempt to stake out the legitimate scope and limitations of psychiatry and decrees the expression of an opinion concerning its benefits and hazards, its blessings and its dangers to the patient. It is a large order.

It is not particularly difficult to discover the surgeon, ophthalmologist or other specialist and to orient him more or less securely in the natural fields of his labors. The psychiatrist is much more elusive and is too often confusingly protean. Now and again one may find him valiantly defending the citadels of endocrinology; mayhap of more sober mien, he may be deeply immersed in abstract psychologic considerations. He may be the concise and businesslike efficiency expert; he may be enlisted in the ranks of child guidance; mental hygiene may have gained his devotion, or psychoanalysis may have wooed and won him. And as for psychiatry itself, from the dim kraepelinian age of somewhat rigid clinical description and diagnosis, it has pursued so many, such diversified and at times such devious pathways that no one can safely predict its future.

I am, however, heartened to my task by two considerations. Fortunately there is a list of agenda, and the chief items for discussion are as follows: In general, what should be the scope of psychiatric practice? Assuming a reasonable amount of organic neurologic training, should the physician who professes to practice psychiatry accept and treat patients who have an organic neurologic disease? Do the psychoneuroses fall within the province of the psychiatrist or of the organic neurologist? What is a neuro-psychiatrist? Should the psychiatrist make a general medical and neurologic survey of psychoneurotic patients? If so, and after he has arrived at a diagnostic opinion, what are the more promising lines of therapeutic attack? Broadly speaking, are these physical or more properly physiologic-therapeutic or psychotherapeutic or more rigidly psychoanalytic? How valuable therapeutically is psychoanalysis, and how important is the place it occupies in the plan of treatment of psychoneurotic and psychotic patients?

What are the relationships of mental hygiene and child guidance to psychiatry, and what should these relations be?

In what degree should the public be "let in" on psychiatry and its ramifications, and what has been accomplished either beneficially or detrimentally through efforts aimed at securing public cooperation? The agenda are scarcely modest, but at least they furnish some limitation.

Furthermore, in this contribution an individual criterion is permitted. I am not required to furnish statistical proof or to inflict questionnaires on practicing fellow psychiatrists but am allowed to survey the field of psychiatric practice from whatever vantage point may have been gained in twenty years of experience in institutional, teaching and private practice. Such a criterion gives a much needed and generous leeway.

THE SCOPE OF THE PSYCHIATRIST

Psychiatric practice is obviously composed of the patients who come to the psychiatrist and belong to the groups that he believes he can legitimately accept for diagnosis and treatment. Naturally, to a considerable degree, such practice is quantitatively and qualitatively determined by the assets, liabilities and professional inclinations of the psychiatrist himself and, of course, it may be made selective and restricted by adherence to the practice of a specialized technic like psychoanalysis. But there is still such a person as the general practitioner of psychiatry. What groups of patients are and should be included in his clientele?

Michael [1] tabulated 200 consecutive records of private patients seen in one year and found the following distribution: psychoses, 41 per cent; psychoneuroses, 28.5 per cent; defective emotional and intellectual states, 4.5 per cent. The remainder was a residuum labeled as "miscellaneous" or "no nervous or mental disease found." Since the general practice of medicine is the sieve through which much of the practice of the psychiatrist is strained, it might be helpful to consider the psychiatric proportion of every-day general practice. Statistics are not presented; yet, in a sense, this statement is statistical. It is founded on the considered opinion of many practitioners and has the additional basis of more than a decade of consultation work. Finally, it is stimulated by reverberations from patients and their families some unsatisfactory years after the onset of what might be termed a psychiatric illness. Somewhat arbitrarily, the psychiatric segment of the general practice of medicine may be subdivided and placed in the order of frequency about as follows: [2]

(*a*) The psychoneuroses and less well defined functional states.

(*b*) Organic disease complicated by neurotic additions.

(*c*) The psychopathologic implications of chronic organic disease.

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1. Michael, Joseph C., in discussion on Thom, D. A.: Psychotherapy in Private Practice, Am. J. Psychiat. **13**:86 (July) 1933.

2. Strecker, Edward A.: Psychiatric Education, Ment. Hyg. **14**:797, 1930.

(*d*) The mental aspects of convalescence.

(*e*) Serious psychopathologic problems in children.

(*f*) Unadulterated psychoses.

With slight modifications and additions this is the practice of the psychiatrist. It is psychiatry. There is a preponderance of neuroses and functional states. The classification of organic disease complicated by neurotic additions is relatively large. The psychiatrist is less apt to come into contact with the problems of mental hygiene in convalescence or chronic organic disease unless they are severe or unusual. Disorders of behavior in children are more frequent in his practice. Frank psychoses are more often brought to his attention. There is the addition of a group of mental defects. Finally, there is an important group which, for want of a better term, can be described only as problems of adjustment. Not only or even chiefly because the patients in these groups are apt to be finally referred to the psychiatrist, but fundamentally because by training and experience the psychiatrist is or should be more satisfactorily equipped to meet their needs than any other physician, these classes of patients belong to the psychiatrist.

NEUROLOGY AND PSYCHIATRY

The next section of the agenda deals with the relationship between the neurologist and the psychiatrist and their orientation in the treatment of patients with so-called nervous and mental diseases. Even if he has the requisite amount of neuro-anatomic knowledge, the physician who professes to practice psychiatry should not accept and treat patients who have an outspoken and uncomplicated organic neurologic disease. By setting down the answer as an emphatic negative the whole question of the validity and usefulness of the traditional association between neurology and psychiatry is brought under fire. Speaking therapeutically, does the psychiatrist obtain from organic neurology any concepts of treatment that are valuable in the handling of his patients? I think not. Practical experience and the weight of authoritative opinion are against this contention. Adolf Meyer may, if he chooses, speak with the authority of an eminent neurologist thoroughly familiar with the structural nervous system. In a recent article [3] he wrote: "With all my love for the structural facts in neurology, I greatly deplore the paucity of help and training offered in the organization of functional data." In the surveys and studies reported in "Psychiatry in Medical Education" [4] little is said of organic neurology, and the stress is placed

3. Meyer, Adolf: Preparation for Psychiatry, Arch. Neurol. & Psychiat. **30:** 1111 (Nov.) 1933.

4. Noble, Ralph A.: Place of Psychiatry in Medical Education, Ment. Hyg. **17:**1, 1933.

on "the development of a closer cooperation between the teaching of psychiatry and that of medicine, surgery and pediatrics." Ebaugh wrote along the same lines.

After all, the opinions of men are subject to change, influenced in varying degrees by their personal experiences. Perhaps a somewhat surer and more scientific criterion may be gained by a brief exposition of the objectives of neurology and psychiatry. Clinical organic neurology as it is practiced is to a considerable extent mathematical and thus often involves the determination of the crossing point of horizontal and vertical lines in the structural nervous system. Now, I am not writing of neurologic research but of actual neurologic practice. Psychiatry, on the other hand, must remain more abstract, dealing with such nonmathematical formulas as the human personality and attempting of necessity to study laws of the mind without direct and constant reference to possible changes in the brain.

After all, the test is one of therapeutics. What has been and is useful for the psychiatrist has been garnered from the field of organic neurology, the rest cure, massage, overfeeding, the sanatorium, the spa and travel; from organic neurology itself is derived no concentration on the life problems and conflicts of the patient, no psychotherapy beyond relaxation, persuasion and suggestion. It must be repeated that no criticism of neurologic research is implied. Conceivably, in its less concrete delvings, possibly along physiologic lines, it may uncover theories and facts of immense value to psychiatry. In the meantime, patients are clamoring at the doors. "Research in neurology and psychiatry serves cultural rather than immediately practical usefulness. Most of the special work of inquiry goes beyond what the individual patient should be forced to pay for." [3]

Inevitably one is led into making a few comments concerning the word neuro-psychiatrist. If intended to denote a neurologist who has the desire to utilize psychiatric attitudes in dealing with the functional aspects of so many of the chronic situations he encounters, it would be a proper word. If intended to signify a psychiatrist who wishes to check as far as is possible without sacrifice of the patient's present needs his psychopathologic concepts and psychotherapy by the structural investigations of organic neurology, the right word would be psychoneurologist. If it means a physician who can alternately and at will either cloak himself in the austere garb of a structural neurologist, testing exactly the validity of the function of the nervous structure and diagnose accordingly, or as a psychiatrist exercise the concepts of psychopathology and the resultant psychotherapy, then it would seem to be a misnomer, the concept which it represents existing so rarely in fact that the hyphen becomes the chief reason for the union of neurology and psychiatry.

THE PSYCHIATRIST AND THE PSYCHONEUROSES

I presume that in the psychoneuroses may be found the larger and more succulent bones of contention. Personally, my thought is that they belong in the province of psychiatry. Functioning as a psychiatrist, how may the physician deal with these serious maladaptations that are so alarmingly frequent in our complex modern civilization? The problem is so extensive that only outlines may be presented. There are choices of therapeutic procedure more or less allied or at least having in common the denominator of psychopathology and psychotherapy, rather than that of neuropathology and physiologic, neurologic or pharmacologic therapy. This does not at all mean that the few available neurologic treatments or pharmacologic concepts should be discarded, but it does mean that if they are the chief source of reliance and dictate the fundamental dynamics of therapy, then such therapy in the present state of knowledge rests on a weak reed. Myerson [5] represents a good exponent of what might be considered advanced thought concerning the physiologic approach in psychiatry. He wrote:

> This approach [the physiologic] to psychiatry and its problems must go logically even further. It must state that there is no separation between the organic and the functional diseases except as a matter of convenience. If I experience fear and, as a result, I become the victim of a psychoneurosis, there is no phase of the experience which cannot be rigidly linked up with the organic world. The object of the situation which evoked the fear is organic. Physical agents of well-defined type, such as light waves, sound waves, chemical emanations which evoke the sense of smell, are organic. Emotion is largely the thalamic, vaso-visceral, motor reverberation of an event. All the past experiences of the individual have been organic, and their effects, whether transitory or permanent, were organic.
>
> Even though we gain no insight into the actual causation of a psychosis or a neurosis by the study of the physical symptoms which accompany it, we are enabled to understand the clinical picture better. We may ask of a mental state, in how far does it disturb bodily function, the great organic machinery of the body? And since it is true that a mental state may alter digestion (by this theory it is in part altered digestion) it is perfectly conceivable that by altering the digestion, we may in turn change the mental state, or, at least, hasten the resumption of equilibrium. In the circle of events which is the relationship of mind and body, therapeutics applied at any point may alter the entire circle.

On the side that draws its ammunition largely from psychopathology and discharges it as psychotherapy, Thom [6] believed that the particular nature of the therapy is conditioned by:

> (1) The personality makeup of the patient, (2) the nature of the symptoms, (3) conditions under which the symptoms were acquired, (4) the purpose they

5. Myerson, Abraham: Physiological Approach to the Psychoneuroses, Bull. Massachusetts Dept. Ment. Dis. **15:1** (April) 1931.

6. Thom, D. A.: Psychotherapy in Private Practice, Am. J. Psychiat. **13:77** (July) 1933.

serve, (5) whether the precipitating cause continues to operate, (6) the method in which the therapist has the most confidence. Finally such factors as employment and finances cannot be ignored.

A method of psychotherapy that embodies much common sense and that is somewhat indebted to the formulations of Meyer may be stated about as follows:[7]

1. *Establishment of Rapport Between the Physician and the Patient.*—This rapport, to be effective, must be based on a certain amount of respect and confidence on the part of the patient. It is best furthered by a careful investigatory program instituted by the physician at the first interview. The more complete the history, physical and mental examination and serologic and blood tests are, the more the patient feels that he can depend on the results of those examinations. The physician must be quite frank in the matter. It is proper to tell the patient that before any final opinion can be given it is necessary to complete the study of his case. This causes no difficulty, provided the physician has outlined a definite investigative procedure and starts the patient on it at once. Any patient is willing to wait for accurate information before the physician begins treatment.

2. *Aeration or Ventilation of the Material of Conflict Presented by the Patient.*—This may be carried out by means of direct interviews, by means of discovering and probing for such material from outside sources, by hypnosis or by any other method. The important thing is that the patient is given an opportunity to discharge and bring out in the open all of those experiences which have been causing him serious concern either consciously or unconsciously.

Desensitization.—This is the procedure wherein the patient is required to face frankly the traumatic and unpleasant experiences of his past. It is brought about in the first place by causing the patient to discuss at frequently repeated interviews the material of conflict elicited as already outlined. These interviews are repeated until the patient can review these experiences without excessive emotional concern. Normal emotivity is to be expected, however, and it is not desirable or necessary to expect a complete loss of emotivity in connection with the events that should normally cause concern. It is the excessive concern that is pathologic and requires to be relieved.

The term desensitization is also applied to the procedure carried out in relieving fear or other manifestations of symptoms in definite situations. The patient is required to face the situation repeatedly until he no longer manifests the symptoms in that situation, or until he is

7. Strecker, Edward A., and Ebaugh, Franklin J.: Practical Clinical Psychiatry for Students and Practitioners, ed. 3, Philadelphia, P. Blakiston's Sons & Co., 1931.

able to tolerate or ignore the symptoms if they occur. It is necessary, of course, to encourage and reassure these patients repeatedly while this procedure is carried out.

4. *Reeducation.*—This is carried out in connection with all the foregoing procedures. It is essentially the development of clear insight on the part of the patient into the mechanism of his illness, the establishment of new habits of response (as in desensitization) and the formulation by him of an adequate industrial, social, recreational and otherwise useful program of activity to insure future stabilization.

5. *Desensitization of the Family.*—In addition to the foregoing, it is often advisable to desensitize the patient's family to his illness and to reeducate them into new habits of response toward the patient.

6. *Remedy of Physical Factors.*—All contributing physical factors are corrected as far as possible. Measures for their correction are instituted at the earliest possible interview and are utilized as psychotherapeutic aids.

The procedures outlined, to be carried out intelligently, require that every individual case be formulated in terms of its causative factors in such a way that the factors that can be modified are emphasized and become the center of attention. Factors which cannot be altered are recognized as such, and the patient is trained to tolerate them.

There is included here a brief and summarized statement concerning the procedure at the well known Stockbridge Sanatorium.[8] The patient is given an opportunity to tell his story in detail. Next, there is a thorough physical and mental examination, followed by a frank discussion with the patient concerning his difficulties and the reasons for his maladaptation. The patient is then informed of the plan of treatment and is given a daily schedule to meet his individual needs. It consists of exercise, diversion and rest. The keynote of the treatment is reeducation. It stresses the importance of dominating the emotions and of utilizing the intelligence as a guide to conduct. Efficiency is emphasized. The patient is impressed with the necessity of making clearcut decisions, at first in trivial, and later in grave, matters. The proper use of the mind is described. The harmful effects of worry, unnecessary hurry, inattention and self-pity are elaborated. They are manifestations of inefficiency. The patient is instructed concerning rest, which is not synonymous with sleep but is chiefly the temporary and volitional abandonment of responsibility.

In the presentation of these statements an answer is furnished, at least incidentally, to some of the leading questions of the agenda.

8. Riggs, A. F., and Terhune, W. B.: Psychoneuroses—Problem in Re-Education, Am. J. Psychiat. **4**:407 (Jan.) 1925.

Do the psychoneuroses fall within the province of the psychiatrist or of the organic neurologist? I believe they are unquestionably within the province of the psychiatrist. Functioning as a practitioner, the neurologist dare not depart far from the structural facts of the nervous system. Naturally, an attitude of mind is induced that cannot deal effectively with the structurally unchecked data of psychopathology and psychotherapy. Presumably, broad neurologic research may eventually offer valuable aid to psychiatry, but the therapeutic exigency that exists and the results of experience both demand that in the psychoneuroses the psychiatrist prefer psychopathologic premises and psychotherapy to the less readily workable and less fruitful therapy produced by organic neurology.

Should the psychiatrist make a general and a neurologic survey of psychoneurotic patients? Not only should he make such a survey, but it is imperative that he do so. It is not a question as to what degree existent organic pathology is instrumental in producing a neurosis or even whether it is influential at all. Usually it is not etiologically dynamic. Nevertheless, somatic morbidity is frequently found on careful examination and therefore careful examination becomes a matter, not of belief, but of conscience and of medical ethics. Adherence to any particular doctrine does not remove the responsibility for determining the actual physical status of the patient.[7]

As to the more promising line of therapeutic attack, it would seem that if the diagnosis of psychoneurosis can be honestly made and substantiated, the treatment should be psychotherapeutic rather than physically therapeutic though, of course, physical adjuncts need not and should not be excluded from the treatment armamentarium. If the converse were under discussion, no one would think of questioning the right of a patient sick with lobar pneumonia to whatever psychotherapeutic help he might derive from the encouragement of his physician, simply because the illness was the result of structural pathology.

Actual details of treatment cannot be discussed in this presentation. Perhaps the important matter of where the patient is to be treated should be mentioned. The determination between the home with regular visits to the office of the psychiatrist and a sanatorium must be made on the bases of the gravity of the neurosis, the seriousness of complicating physical factors and the possibility of a reasonable control of environmental factors, and to some extent it must be controlled by the economic situation.

Psychotherapy in its modern sense presupposes the acceptance of at least a minimum of psychopathologic doctrine. It is extremely difficult and hazardous to state what such a minimum implies. Many of the signs and symptoms familiar to the organic neurologist, for instance, sensations, have representations in the consciousness of his patient. In a

sense therefore he studies minds, of the contents of which the subjects are clearly aware, and he studies and questions his patients chiefly from the standpoint of elucidating the findings obtained in his examination. The psychiatrist studies another mind, the content of which the patient does not clearly perceive, though I am convinced that much of the content that is important in the therapy of the neuroses is nearer the threshold of consciousness than is commonly believed by psychoanalysts. Some of the rather far flung boundaries of this mind described by several of the disciples of Freud seem to be more fantastic than real and, even if defensible along phylogenetic lines, it is unlikely that such theories are of material aid in the practical therapy of the psychoneuroses. Nevertheless, there is a not-conscious mind, the investigation of which is profitable to the psychiatrist, since it contains a record of what has happened to the person during his lifetime.

As in organic neurology a surface sign, for instance the eyeground picture in tumor of the brain, may be a clue to an underlying and significant pathologic process, so many so-called surface neurotic signs and symptoms and other less clearcut phenomena may strongly suggest a deeper psychopathologic condition. For convenience, "complex" may be used to denominate somewhat obscured material that is emotionally dynamic and persistent enough to demand expression in the every-day life of the person. Some of this complex material has been accumulated as a result of the reaction to psychically traumatizing experience and its subsequent repression. When such strong complexes lead to tendencies and desires not satisfactory to the self-criticism of the subject and usually not acceptable in the judgment of the majority of others, that is of the herd, there is apt to be conflict. Many psychoneurotic patients come to the psychiatrist at the stage when the respective demands of their ego, sex and herd complexes have become irreconcilable for them and their symptoms constitute a pathologic attempt to minimize or subdue the inner psychic conflict.

While the limits of this paper will not permit detailed discussion, it is obvious that there is some connection between what has been written and the development of human personality. In the psychiatric attitude and approach, personality is the outstanding target for investigation and therapy. Not forgetting at all its hereditarial and somatic influences, one may state that it is the condensed record of the person's lifetime experiences and reactions thereto. It is highly important, therefore, to know what has gone into the making of the personality, and also to scrutinize it carefully for potential weapons that might be forged and shaped into weapons potent enough to be utilized in the attack on the real problems of life temporarily obscured by the neurosis. Inevitably, personality brings up the question of environment. In a given patient,

no real psychiatric understanding can be won without appreciation of the tremendous part that has been played in the past, and the influence that is now being exerted, by environment, not only in its broad, material sense, but even in its most minute and personal implications. All this is simple, and, perhaps, ridiculously elementary, but it may serve the purpose for which it is intended, that is, to show why neurology and psychiatry, at least so far as they view the psychoneuroses, cannot expect to go hand in hand and must accept many points of departure in the conception of pathology and the application of therapy.

PSYCHOANALYSIS AND PSYCHIATRY

Unfortunately, the agendum covering this point asks a very direct question. How valuable therapeutically is psychoanalysis (it is understood that formal psychoanalysis is meant) and how important is the place it occupies in the treatment plan of psychoneurotic and psychotic patients? The discussion may be opened by stating that formal psychoanalysis necessarily occupies a very restricted rôle in the therapy.

Fortunately, it may be a discussion and not an argument concerning the intrinsic validity of psychoanalysis. The day of bloody verbal battles between analysts and nonanalysts is over. The last and silencing gun was fired by the analysts when they asserted that the psychoanalytic doctrine cannot be understood without the experience of a successful personal analysis. Since this implies acceptance and conversion, all controversy is automatically terminated. The premise—no analysis, no understanding—is impregnable.

Freely, the debt of psychiatry to psychoanalysis should be acknowledged: It inspired a turning away from what had become a narrow, restricted, objective and descriptive psychiatry toward a broader, more subjective and more interpretative point of view; it emphasized the value of mental catharsis; it supplied explanations of psychopathologic mechanisms, underlying symptoms—always interesting and occasionally valid—and it offered a technic of psychotherapy applicable to a limited segment of psychiatric practice.

It is difficult to form a just opinion as to the boundaries of this limited segment of psychiatric practice. Meyer [8] believed that "psychiatry is much broader than psychoanalysis" and that the latter "as an incident in the broader training is to be limited to the specially talented physicians and well chosen patients, and is not to figure as the all-pervading principle of nonpsychoanalytic practice." Thom [6] apparently found large groups of patients for whom formal psychoanalysis does not offer a very promising therapy:

> For the psychiatrist who is seeking the most practical method of rendering aid of a valid sort to the ever increasing number of individuals who are seen in private

practice and at clinics, I know of no one question which is so demanding of an answer or so helpful in the solution of the problem as that of 'What purpose does the neurosis serve in the life of the individual?'

I believe that there is a very direct relation between the ability of the psychiatrist to answer this question correctly and the success of his therapy. I am not forgetting for a moment that after the purpose of the neurosis has been revealed, we must then go on and either establish in the mind of the patient the futility of this purpose or see that this purpose is met in some substitutive way. From my own personal experience I am of the opinion that many of the conflicts of our patients are not deeply buried in the mire of early experiences, but bear a close relation to the existing problems of their every-day life and that many of these conflicts are due to social and economic factors which are all too frequently just without the reach of psychiatric technic per se. What many of our patients need is a philosophy of life which will permit them to get their problems focused so that they may view them objectively and in their proper perspective.

It is fair to observe formal psychoanalytic therapy from the actual experience of psychiatric practice. Statements that might appear too empirical have, after all, been checked by actual observation. Thus, psychoanalysis is rather rigid in its prescribed formulas and technic and does not admit of much modification. It has little if any usefulness in the actual treatment of psychotic patients and in a few psychotic situations, as for instance, incipient and early schizophrenia, in which certain psychoanalytic concepts should be helpful, psychoanalytic therapy can scarcely be applied unless it is considerably modified. By its very nature, psychoanalysis is not able to deal in a practical manner with the many exigencies and even crises of daily psychiatric practice. Psychoanalysis is not adapted to short cuts and, therefore, it offers no feasible method of treating the many psychic bruises and sprains (as for instance certain types of overreaction to masturbation in adolescents) that may often be healed in a comparatively short time by aeration, desensitization and explanation. Finally, many patients are returned to the general psychiatrist, obviously not at all helped by the analysis. Naturally, any method of psychotherapy may eventuate disastrously.

There is a small fraction of patients, falling chiefly in the psychoneurotic group, that should probably be referred for psychoanalysis. When the neurotic symptom-complex constitutes a serious disability and when other methods of psychotherapy leave it untouched, then, after proper explanation to the patient, and furthermore when no contraindication to analysis exists, this method of therapy should be recommended.

PSYCHIATRY, CHILD GUIDANCE AND MENTAL HYGIENE

It is too early to evaluate with any exactitude the value of child guidance. It has accomplished a great deal, but it must still make itself

even more serviceable, not only to psychiatry but also to pediatrics. Veeder [9] wrote:

> The "child guidance" movement is one that interests the pediatrician intensely, and I believe that it is more nearly related to pediatrics as a whole than to psychiatry. Pediatricians have watched it closely and have taken part in it with the hope that it will eventually be a pathway to better things. Those who for many years have been closely associated with the child hygiene movement have seen a marked parallelism between the two. The chief fault of the child guidance movement has seemingly been its intense desire to prove something rather than to find out something and to look on its methods as fixed rather than experimental. Not many years ago I heard one of the chief exponents of the movement state that the "child guidance clinic would eliminate child delinquency in a few years." He would be the first to laugh at such a statement today. In child guidance, as was the case in earlier infant welfare work, there is a confusion between principles and methods. The child guidance clinic is only a method. When one pictures the evolution and change of the infant welfare clinic or health center in the past twenty years, the description of the present child guidance clinic as a "classic" unit brings a smile. I have every reason to believe that the child guidance clinic is being and will continue to be an important factor in bringing about a better understanding and in turn a better handling of the problems of childhood. Its chief fault has been its isolation. As the pediatricians have come to see the problem, its chief value lies not in its existence as a separate unit or field but rather in the possibilities for its close incorporation into the complete medical program for the child. While isolated units may be needed for specific purposes, as in the schools for educational problems or in association with juvenile courts, the most important place of the clinic is in the medical school, in intimate association with medical education. Only in this way can it influence the thought and attitude of physicians, and in the ultimate analysis this is the only method by which help in problems of conduct and behavior can be given to the millions of children in America. Child guidance clinics, like infant welfare clinics, can reach directly only a very small number of persons.

As a practical method of therapy child guidance in the clinic will have difficulty in justifying itself, since not only does it tend to become too isolated but it is too expensive. Furthermore, while something is gained by larger facility and more exact technic, undoubtedly something is lost in the direction of relationship between child and psychiatrist. It would seem a fair forecast to write that the contribution of child guidance to pediatrics, psychiatry and medicine in general will be not so much as a treatment center, meeting the problems of large numbers of children, but as a laboratory of study and, in a limited sense, therapy, with a teaching function and with free avenues of access to psychiatrists, pediatricians and other physicians, so that important information that has been gained may be readily imparted.

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9. Veeder, Borden S.: Training of Neurologist, Neuropsychiatrist and Pediatrician, Arch. Neurol. & Psychiat. **30**:628 (Sept.) 1933.

Mental hygiene [10] is on trial. It deserves to be on trial. It has been overpropagandized, overdramatized and oversold, so that now it is in the unfortunate position of being obliged to default in some of the dividends that it has so lavishly promised.

If it can find and keep within its rôle, mental hygiene has a most important contribution to make. It would seem a fair criticism that mental hygiene has busied itself too much with abstruse and highly speculative considerations and has failed to take proper cognizance of the limitations of psychiatry.

It should define its objective more clearly. Life has not only a physical objective but also a psychologic objective. The former is well understood and comparatively rather well accomplished, so that, on the whole, the physical machinery works more efficiently and is longer lived than formerly. The psychologic objective should not be much more difficult to comprehend. Broadly stated, I presume it is the capacity to become adjusted, to give and take, to maintain a satisfactory balance between self and environment. Man is gregarious, and within limits it is demanded of us that we live within a social state. Furthermore, man is competitive, often starkly so, in spite of the veneer of civilization. Therefore, when the child passes from childhood to adult life he steps on a somewhat social, somewhat competitive stage. Common sense hygiene would seem to indicate that he be properly prepared, and the home and school should be the agencies in which a balance of social adaptation and independence are taught and practiced. Parents and others who stand as surrogates for the parents should be the teachers, and in back of them should stand the physician. The point has been reached where the physician must be and should want to be not only the man who orders a milk formula and vaccinates, not only a counsellor of physical health but also, and very definitely, the counsellor for mental health.

Before this can be accomplished it is necessary to depart somewhat from a strict consideration of the mind as being solely and restrictedly the function of a structural brain. There must be accepted, appreciated and utilized, for instance, such nonstructural conceptions as personality, into the making of which there has gone much material and experience that is no longer clearly apprehended consciously. If there is a mind the content of which is not open at once to every-day conscious scrutiny, then obviously any part of the content that is harmful may have been taken in earlier in life in the shape of misinformation, often emotionally disturbing or even traumatizing, concerning vital facts of life and living. Furthermore, the material was never mentally digested. One would

10. Strecker, Edward A.: Psychiatry and the Practice of Medicine, read before the Philadelphia County Medical Society, October, 1933.

scarcely expect to produce an efficient physical machinery under the plan of ingesting poisonous or unsuitable food into the body and permitting it to remain and act as an irritant. Some application of the derivatives of such thinking in attempting to direct the growth of minds of children might well be a first principle of mental hygiene. Many persons when the paths of their lives bring them face to face with a difficult place, in other words, when they are in conflict, cannot weigh the respective claims of the conflict consciously, but develop certain functional symptoms that are protective but pathologic and dangerous. Life will be hard on every person. Experience shows that he must expect to be placed from time to time in trying and even desperate situations. If their underlying components can be recognized (with help if necessary) and faced openly and fairly and a decision made, then, even if it is a faulty decision, it will still be better for the hygiene of the mind than psychologic camouflage. Mental frankness can be taught best, and perhaps only, in childhood. The small affairs of children should be the testing ground for the development of mental habits that will work satisfactorily in the affairs of adult life. There are many other factors, but they cannot be considered in this presentation. When physicians begin to apply them there will be real mental hygiene.

In a broad sense many of the maladaptations, neuroses and minor psychoses are protests of the person against the social scheme. Naturally, any one has the right to protest, but the protest would be the more legitimate and the more effective if the person had been properly prepared in childhood for adult life.

If one third of the amount of attention that is now given to the bodies of children were given to their minds, there would eventually be a decrease of mental illness and maladjustment and an increase in efficiency, adjustment and happiness. It may be repeated that there is available a small, but nevertheless concrete and important body of information that ought to be utilized just as freely in the training of children as are the laws of physical hygiene.

There remain only a few considerations in the agenda, and they revolve largely around the relation of the psychiatrist and of institutions for mental disease to the public. Should cooperation be encouraged? Should the psychiatrist and the institution, one or both, embark in the education of social groups in mental hygiene and social psychiatry? Have the attempts so far made been successful? Have radio talks been of any value?

The answers to these and similar questions and, indeed, the fundamental issue at stake in the education and attempt to enlist the cooperation of the public concern the kind of information that is issued in books and pamphlets or by lectures or radio talks. What have been our

sins of omission and of commission? I believe that we have failed to impart, emphasize and reiterate both in psychiatry and in mental hygiene the simple and well known facts and have spent much time in giving forth abstruse and complex speculations, highly interesting, but often unproved, rather sure to be misapplied and, indeed, not ready for application. For instance, if properly discussed it is valuable for the public to know that the spirochete may cause dementia paralytica. It is of dubious value and may lead to much unhappiness to retail the freudian theory of dreams. It is good public education to advise that certain well known potentials of mental growth, such as imitation, suggestibility and curiosity, be developed and utilized in childhood or that the goal to be accomplished is the balance between independence and socialization, yet I doubt whether such objectives can be accomplished by expounding at length on "fixations" and Oedipus and Electra complexes. In other words, we have a body of information to impart that is about equivalent to the basic, common sense teachings of physical hygiene concerning food, fresh air, sunshine, care of the teeth, etc. The day may well come when such progress will have been made in psychiatry and mental hygiene that correspondingly more complex information may be advantageously released for public consumption, but there must be a bit more factual evidence before we can instruct the public much beyond the few known and still sorely needed simple lessons of mental health. "It is quite probable that for some time to come a reasonable amount of continence in publication is more of a virtue than a cause for reproach. Particularly in the direction of 'mental hygiene,' publicity and promises of therapeutic booms, a more conscientious adherence to what can be proved and used is greatly to be desired." [3]

111 North Forty-Ninth Street.

News and Comment

AMERICAN NEUROLOGICAL ASSOCIATION

The sixtieth annual meeting will be held from June 4 to 6, 1934, in Atlantic City, N. J.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The next session will be held in Christmas week, 1934, at the Hotel Commodore, New York City. The subject will be "Sensation and Sensory Disturbances." The chairman is Dr. T. H. Weisenburg, 1930 Chestnut Street, Philadelphia. Authors are invited to submit clinical or clinicopathologic papers dealing with this subject.

The topic for 1935 is to be "Neoplasms of the Nervous System." Dr. Edwin G. Zabriskie, 115 East Sixty-First Street, New York City, is the chairman in charge of this program.

MEETING OF PROGRAM EXECUTIVE COMMITTEE, SECOND INTERNATIONAL NEUROLOGICAL CONGRESS

The meeting was held on Sept. 6 and 7, 1933, in London. On the evening of Wednesday, September 6, a formal reception was held at the Royal Society of Medicine which was attended by many of the delegates and their wives. The delegates were received by Mr. Warren Low, the president of the Royal Society of Medicine, and Dr. Risien Russell, the president of the Section of Neurology of the Royal Society of Medicine. During the reception a meeting of a number of delegates was held to arrange informally for the presentation of a list of nominations for the officers of the congress to be held in 1935. This meeting was presided over by Dr. Sachs, president of the First International Congress, and was attended by Drs. Brouwer, Dubois, Foerster, Holmes, Lhermitte, Marburg, Riley, Rossi and Wilson.

The meeting of the delegates to the Program Executive Committee was called to order at 9:30 a. m., September 7, Dr. B. Sachs in the chair. The following delegates were present: Drs. R. Morea and B. Odoriz, Argentina; Drs. O. Marburg and G. Stiefler, Austria; Dr. L. van Bogaert, Belgium; Drs. Munch-Petersen and E. Sörensen, Denmark; Drs. C. Baudouin and J. Lhermitte, France; Drs. M. Nonne and O. Foerster, Germany; Drs. Gordon Holmes and Kinnier Wilson, Great Britain; Drs. C. U. A. Kappers and B. Brouwer, Holland; Dr. L. Benedek, Hungary; Drs. O. Rossi and V. M. Buscaino, Italy; Drs. I. Lossius and G. H. Monrad-Krohn, Norway; Drs. E. Moniz and A. Lima, Portugal; Drs. C. Dubois and R. F. von Fischer, Switzerland; Drs. B. Sachs and H. A. Riley, United States.

The following delegates were appointed, but were unable to attend the meeting: Drs. H. Prochazka and J. Sebek, Czechoslovakia; Dr. M. Catsaras, Greece; Dr. A. von Sarbó, Hungary; Drs. H. Halban and W. Sterling, Poland; Dr. G. Marinesco, Rumania; Drs. G. R. Lafora and R. Arias, Spain; Drs. H. Marcus and N. Antoni, Sweden; Prof. Austregesilo and Dr. O. Gallotti, Brazil; Dr. Y. L. Wei, China; Dr. Y. Barrada, Egypt; Prof. Puusepp, Esthonia.

The minutes of the meeting of the Program Executive Committee of the First International Neurological Congress, held in Bern in September, 1931, were read. It was decided that the name of the next congress would be the "Second International Neurological Congress."

Nominations were then made for officers for the Second International Neurological Congress. The nominations were as follows: honorary president, B. Sachs; president, Sir Charles Sherrington; deputy president, Gordon Holmes. Nominations for vice-presidents were: Emanuel Balado, Argentina; Otto Marburg, Austria; Auguste Ley, Belgium; A. Austregesilo, Brazil; Colin Russell, Canada; Ladislav Haskovec, Czechoslovakia; Vigo Christiansen, Denmark; Henri Claude, France; Otfrid Foerster, Germany; Bernardus Brouwer, Holland; Karl Schaffer, Hungary; Ottorino Rossi, Italy; G. H. Monrad-Krohn, Norway; Orzechowski, Poland; Egas Moniz, Portugal; G. R. Lafora, Spain; Henry Alsop Riley, United States. Japan, Rumania and Russia are to be consulted as to their choice of a representative to serve as a vice-president.

Nominations for other officers were: secretary-general, S. A. Kinnier Wilson; assistant secretaries, Macdonald Critchley and E. A. Carmichael; treasurer, Anthony Feiling; editor of the Transactions, Gordon Holmes; assistant editors, Rodrigues Arias, Spanish, Vito M. Buscaino, Italian, Charles Dubois, German, J. Lhermitte, French.

The Program Executive Committee Meeting then proceeded to the discussion of the plans for the meeting of the Second International Neurological Congress. It was decided that the Congress should be held in London during the week of July 29 to Aug. 2, 1935. A program committee consisting of the British officers of the Congress and the chairmen of the stated programs was appointed to arrange the program of the Congress.

It was decided to follow the same general arrangement as existed for the First International Congress, devoting Monday, Tuesday, Thursday and Friday to scientific sessions and reserving Wednesday for nonscientific activities.

Four stated topics were selected to be presented during the morning sessions, the afternoon sessions being left for miscellaneous topics, the number of sessions to be determined by the total number of papers accepted. The following topics, with the chairmen to whom the preparation of these programs for the stated sessions was assigned, were chosen: "The Epilepsies: Etiology, Pathogenesis and Treatment," Otto Marburg and Ottorino Rossi, chairmen; "Physiology and Pathology of the Cerebrospinal Fluid," Otfrid Foerster, chairman; "The Functions of the Frontal Lobe," Henri Claude, chairman; "The Hypothalamus and the Central Representation of the Autonomic System," Bernardus Brouwer, chairman.

It was decided to devote two sessions to the epilepsies, and Monday morning and afternoon, July 29, were tentatively chosen for the presentation of this subject.

It was concluded that the chairman preparing the program for each stated subject should select five chief reporters, but that eight chief reporters should be selected for the program on the epilepsies. Each chief reporter will be allowed twenty minutes for the presentation of his contribution. The chairman preparing each stated program may select five persons who will present a formal discussion of the papers presented, and after they have spoken, discussion will be thrown open to the floor, each discusser in the open discussion being allowed five minutes for his remarks.

It was decided that abstracts or outlines of contributions on the same stated program should be furnished as early as possible to the chairman for each stated program, for distribution to the other reporters on the same subject in order to prevent overlapping in the preparation of the contributions.

Abstracts for incorporation in the program must be submitted to the program committee by March 1, 1935. Completed papers for the stated sessions must be in the hands of the program chairman and the program committee by March 1, 1935.

The meeting then proceeded to a discussion of the arrangements for the sessions devoted to the presentation of miscellaneous papers. The choice of chairmen for these sessions will depend on the number of sessions required and therefore on the number of papers submitted. The presiding officers for these sessions will be chosen from the vice-presidents or from other distinguished members of the Congress. The program committee was entrusted with the choice of these chairmen.

It was decided that each member of the Congress is entitled to present one paper, but the program committee was authorized to consider each suggested contribution and to decide on the merits of the contribution and whether it should be presented before the Congress or not. Not more than one contribution from any one author will be allowed, but members of the Congress invited to participate in any of the set subjects may present one other paper of a miscellaneous character. No presentation shall exceed ten minutes.

The arrangement of the sessions will be carried out as far as possible in accordance with the subject matter of the papers, papers of a similar character being grouped together in one session. It was decided that there should be free discussion following each paper, each discusser, however, to be limited to five minutes for his remarks. Abstracts and final copies of papers submitted on miscellaneous subjects shall be in the hands of the program committee by March 1, 1935.

A discussion of the types of membership in the Congress resulted in the decision to enroll honorary, active and associate (affiliated) members. Honorary members were proposed by the Program Executive Committee as follows: Ramón y Cajal, Henry Head, Fedor Krause, Pierre Marie, G. Marinesco, L. Minor, J. P. Pavlov, F. Schultze, A. Souques, E. Tanzi, A. von Eiselsberg, J. W. von Jauregg, William H. Welch and C. Winkler.

Candidates for active membership may make application in one of two ways: either through one of the national committees, in which case their qualifications shall be examined by the national committee, or by direct application to the Program Executive Committee through Dr. S. A. K. Wilson, its secretary, in which case their qualifications shall be examined by the Program Executive Committee. Membership cards for all members of the Congress shall be issued by the secretary of the Congress, and payments shall be made either through the national committees or directly to the treasurer of the Congress.

The associate (affiliated) members shall consist of nonprofessional interested persons.

The question of the financial support of the Congress was then discussed. It was decided to request each national organization to appropriate certain sums for each of the two years, 1934 and 1935, for the support of the Congress as follows: $100, or its equivalent in Swiss francs, France, Germany, Great Britain, Italy, United States; $50, or its equivalent in Swiss francs, Austria, Holland, Switzerland; $25, or its equivalent in Swiss francs, Argentina, Brazil, Belgium, Hungary, Poland, Rumania, Spain and the Union of Soviet Socialist Republics.

This arrangement was based on the numerical membership of the First International Neurological Congress as follows: 50 or over, Great Britain (51), France (95), Germany (85), Italy (92) and United States (160); from 25 to 50, Austria (25), Holland (34) and Switzerland; from 10 to 25, Argentina (14), Brazil (17), Belgium (17), Hungary (19), Poland (20), Rumania (14), Spain (12) and Union of Soviet Socialist Republics (14). No decision was reached as to the contribution to be expected from the countries whose representatives numbered less than 10, among whom were: Canada (5), Czechoslovakia (9), Denmark (5), Japan (5), Norway (6), Portugal (7) and Sweden (9). The date of payment for these assessments was decided on as Jan. 1, 1934 and Jan. 1, 1935.

It was decided that the equivalent of 25 Swiss francs should be the fee for active membership in the Congress. The fee for associate membership was fixed at the equivalent of 12½ Swiss francs.

The question of the official languages was then discussed at considerable length. It was finally decided to recognize five official languages: English, French, German, Italian and Spanish. It was further decided, however, that in order to limit the expense of publication, abstracts for incorporation in the official program by contributors speaking in Spanish or Italian would have to be submitted in any one of the three languages English, French and German.

It was decided that the question of the arrangements for the housing of members and the appointment of a committee on publicity should be left to the British committee.

It was decided that Thomas Cook and Sons should be the official travel agency for the Congress.

It was unanimously decided to send a message of greeting to the new president, Sir Charles Sherrington.

After various expressions of appreciation to the officers of the First International Neurological Congress and to the hosts of this meeting of the Program Executive Committee of the Second International Neurological Congress, the meeting adjourned. On Thursday evening, September 7, the delegates and their ladies were entertained at the Dorchester Hotel by the Section of Neurology of the Royal Society of Medicine, Dr. Risien Russell presiding.

HENRY ALSOP RILEY, M.D., *Secretary-General*
of First Interational Neurological Congress

Abstracts from Current Literature

PERIPHERAL NEURITIS; THE MORISON LECTURES, 1932. JAMES COLLIER, Edinburgh M. J. **39**:601, 672 and 697, 1932.

Collier's long experience and profound thought on the subject of peripheral neuritis makes this epitome of extraordinary value and interest. Taking as his main theme the infective polyneuritides, he assembles practically all other known types, showing their interrelationships and drawing conclusions that are far-reaching in value. Epidemics of peripheral neuritis were known in the past century by Robert Graves, and have been set apart as nosologic entities by Grainger Stewart, Jackson and others. Ross and Bury did much to codify the existing information, and to point out the following significant criteria: Spasm is a characteristic feature, whether it be represented by fibrillary twitching or massive tetanic seizures; involvement of every level of the nervous system is observed (e. g., in Korsakoff's psychosis); Landry's paralysis is typical of neuritis advancing "by tissue continuity and without discoverable histologic change, and when not fatal, rapidly and completely recovering." It was a long time, however, before the differentiation of toxic neuritis from infective neuritis was established. Indeed, Duchenne de Boulogne, though he spent his life studying the peripheral nerves and muscles, had no use for peripheral neuritis, and the discovery of the lesions of poliomyelitis only confirmed him in his opinion.

The concept of "multiple symmetrical peripheral neuritis" was brought forward by Grainger Stewart in 1881. He believed it to be due to a poison circulating in the blood, either derived from without by ingestion or within the body by infection, and that this poison affected the periphery of the longest nerves first and most, because it was thought that the nutritional influence of the nerve cell and its nucleus was lowest at the most distant part of the nerve fiber. According to the concentration of the poisoning agent and to the duration and depth of its influence, the damage extended to the shorter nerves and might become universal. Nevertheless, a physiologic selective capacity on the part of the poison for the nerves of the several regions had of necessity to be accepted to explain the varying distribution of the paralysis both with different poisons and with the same poison. Joffroy introduced the differentiation between parenchymatous and interstitial neuritis, although Collier considers this separation unsound. One of the more recent phases of the subject is the recognition of distinct changes in the spinal fluid in cases of neuritis, particularly in those in which the etiology remains in doubt. So far as the nerves themselves are concerned, the alterations are always a mixture of the degenerative and the reactive type, although variations are found from one end (pure degeneration in lead poisoning) to the other (pure reactive interstitial changes in sciatica).

The toxins of multiple neuritis show strong indications of traveling by the axon itself. This has often been demonstrated in connection with rabies and with wound tetanus, and is seen characteristically in paralysis of the palate and pharynx in diphtheria. That the perineural lymphatics are not concerned is seen in the failure to reproduce rabies in an animal by the gentle inoculation of a weak virus into the nerve trunk, whereas if force is used and the axons are ruptured, the characteristic disease will supervene. The concept of rabies as a peripheral neuritis with later dissemination through the central nervous system is held proved by the many examples of "dumb" rabies; and of tetanus as a similar affection by the numerous cases of flaccid paralysis with later recovery occurring in treated persons. The local spasm in tetanus is considered to be a manifestation of direct local action by the toxin on the peripheral nerves, a reversible condition since there may be complete recovery, and since it yields no significant histologic alteration. Collier includes, as examples of peripheral neural disturbance, the immediately

reversible states of flaccidity and of spasm in beriberi and in tetany, and concludes his first lecture with animadversions on the epidemic of ginger paralysis observed in the United States, insisting on the commencement of the condition with tetany-like spasms, and on the variation in the clinical manifestations, ranging from tetanoid spasms in the rabbit to jerkless paralysis in the calf.

The delivery through the blood stream of a quantity of poison to the nerves and their endings determines the classical widespread peripheral neuritis. However, it has been shown by Aub that the concentration of lead rises in muscles that are about to be paralyzed, and Collier believes that the spasm attendant on local neuritis may indicate a purely muscular event. Tenderness of muscles and pain are referred to this accompanying involvement of the neighboring structures rather than of the nerves themselves, and the contracture that may follow is an expression of cicatrization of these lesions rather than of the neuritis itself. A characteristic example of such combined involvement is seen in so-called neurodermatomyositis, first described by Gowers. No primary neural degeneration or exotoxin fixation, and no pressure on nerve trunks causes pain. "For peripheral neuritis to be of the painful form there must be one or both of two lesions added to the neuronic lesion. There must be either an interstitial lesion outside of and irritating the sensory nerve terminals or there must be an interstitial lesion of the nerve trunk."

Remarkable indications of the conveyance of the virus along nerve pathways are to be found in experimental poliomyelitis. After nasal inoculation the virus may be found in the olfactory tract on the same side, in the same pyramidal tract, crossing over with the decussation to involve the lumbar cord on the opposite side, with paralysis of the contralateral hindlimb as the first manifestation of the active disease. The virus can easily traverse the synapses; yet it is unable to cross breaks produced artificially in the peripheral nerves. On its course it leaves the characteristic oxyphil inclusion bodies that "have been proved to be little balls of encysted virus since they resist tryptic digestion; and by such digestion the enclosing tissue can be dissolved away, the inclusion balls swung out with the centrifuge, demonstrated under the microscope and found to be highly virulent infecting agents when inoculated into another animal."

The specificity of the viruses in their attack on certain portions of the nervous system is typified by the wholesale destruction of the cerebellar neurons in louping ill, with integrity of all other cell systems in the nervous system. Similar examples are not wanting in pathologic conditions in man. In herpes zoster, antibodies can invariably be recovered, indicating that the infection is present before the local trauma sets in operation the disintegration of the nerve tissues. The virus then travels along the peripheral extension of the affected nerve unit and produces the characteristic cutaneous eruption. That spread through the blood stream is possible is indicated by the development of a generalized eruption resembling varicella. The pain in herpes zoster is due to the inflammatory lesions along the course of the undegenerated nerve fibers. Painful poliomyelitis has been proved to be associated with intense inflammatory changes about the regional nerve trunks. In some instances, peculiar distributions of the eruption, of the pain and of the paralysis in herpes zoster indicates involvement of several ganglia, possibly on opposite sides of the body. Many instances of Bell's palsy are in all probability due to zoster without eruption. A final proof of nerve transmission of virus is cited in the appearance of the rabic virus in the saliva after inoculation into the brain.

Collier then turns to the recent observations on infective multiple neuritis. The memorable results of Bradford, Bashford and Wilson during the World War have not been repeated. These investigators recovered a virus in some of the thirty cases of infective polyneuritis, and transmitted it in series to animals. The neuritis that is occasionally observed in many of the specific fevers is probably not the direct result of the fever, but that of an additional agent. This excludes, of course, the well known exotoxin neuritides of diphtheria and tetanus, and refers particularly to the endotoxin activities of typhoid fever and the like. Moreover, the clinical picture is usually not that of true polyneuritis.

Whether toxic neuritis results from the action of the poison alone, or from some metabolic disturbance or deficiency caused by the poison, or by the exclusion of important substances from the diet cannot be altogether decided. Alcoholic neuritis has occurred after a single large dose, and arsenical neuritis may follow acute poisoning. Single doses of lead apparently do not cause neuritis, yet inadvertent intravenous injection of bismuth, as in a case observed by the author, was followed by convulsions, delirium, hemiplegia, temporary blindness and finally by generalized flaccid paralysis and eventual recovery. The exacerbation of lead paralysis following an acute illness or dietary indiscretion is explained on the known facts that lead is stored in an insoluble form in the bones, but that resorption of bone from whatever cause throws into the blood stream an overwhelming dose of lead that rapidly causes degeneration of the peripheral nerves. Madame Dejerine has described lead neuritis in several different forms, sometimes as imitating Landry's paralysis. The Manchester epidemic of neuritic paralysis, which did such harm to the brewing trade, was originally believed to be due to the arsenic that contaminated the beer, but Collier believes that it was similar to the epidemics of unknown cause that have been observed before and since, and that arsenic was not to blame.

The involvement of the cranial nerves is characteristic of certain epidemics. In some the oculomotor apparatus is affected; in others the facial or lower bulbar nerves. The absence of pain in the muscles indicates a primary neural involvement, with no significant spread to the interstitial tissues, and the course is usually favorable, even when alarming symptoms become manifest. The spinal fluid is usually normal, but a peculiar brownish color with large quantities of protein and spontaneous coagulation are sometimes observed.

The final iconoclastic remarks of the second lecture concern the neuritic manifestations of subacute combined degeneration of the spinal cord in pernicious anemia. One of the earliest and most striking symptoms is the paresthesias in the extremities of the limbs. "As the disease progresses these sensations advance up the limb and are followed by loss of sensibility of true peripheral distribution, and always remaining of the stocking and glove order. The loss is to all forms of sensibility. In the end, in some of the cases, there is a peripheral atrophic paralysis. The well-known lesions of the spinal cord cannot possibly account for this strict peripheral distribution of the sensory phenomena." The changes are apparently due to a demyelinating form of peripheral neuritis; and the relief of subjective symptoms in patients adequately treated, with persistence of all the objective signs of damage to the spinal cord but with abolition of the stocking and glove anesthesia, indicates that the peripheral disturbance has been overcome.

Certain other diseases of the spinal cord are associated with neuritic manifestations, particularly Morvan's disease and syringomyelia. That these are not the same disease is insisted on by Collier. Whether peroneal atrophy is sometimes or always a neuritis is questioned by the author. The neural changes in diabetes are particularly interesting. The commonest variety is the interstitial neuritis giving a picture of sciatica or lumbago. The effect of insulin is often dramatic. Another variety is the rapid and painless onset of complete and irrecoverable paralysis of one or more of the large peripheral nerve trunks. This is supposed, with good reason, to be due to thrombosis of the artery supplying the nerve trunk itself. The rarest type is the paralysis of the extra-ocular muscles, sometimes associated with retrobulbar neuritis. The rapid recovery in many of these cases may indicate a local edematous involvement of the nerve trunk. Finally, a generalized peripheral neuritis may occur with trophic disturbance and atrophy, ataxia and peripheral paralysis.

Among the most curious manifestations of multiple neuritis are those in which the spinal fluid shows a characteristic and marked departure from the normal. The Froin syndrome has already been mentioned. Sometimes there may be sufficient interstitial neuritis to bring up the question of metastatic involvement of the nerve roots or spinal cord. There is a strong probability that in these cases there is predominant involvement of the spinal roots within the dural membrane.

Neuritis of relapsing type, relatively painless, is often due to an unrecognized infection with the Klebs-Löffler bacillus, and eradication of the focus is followed by complete recovery. In some cases, however, the neuritis may proceed by stages to an eventual fatality. In such instances, during the early progressive phases, there may be marked increases in globulin in the spinal fluid, with only a few cells; but in the stationary phases, the albuminocytologic dissociation disappears and does not reappear in the final, rapidly advancing, fatal process. The globulin in such cases may be considered as an indication of the reacting mechanism, active when resistance is high, absent when the process is not advancing, and suppressed when it is finally overwhelmed.

Fever is a variable phenomenon in peripheral neuritis, even of the infective type. It is usually absent in Landry's paralysis, but is often present when cranial nerves are affected. Fever has no particular prognostic import.

Traumatism to nerves is not uncommonly followed by very severe painful manifestations. Fine tremors are often engendered in the fingers by the agonizing pain. Even forceful stretching may produce this result, together with an ascending interstitial inflammation of the whole nerve trunk. The same process may be the one responsible for causalgia, but in such cases the ordinary septic processes are not concerned, and nearly all cases eventually end in recovery.

Typical cases of neuritis of various forms are so common that one is prone to overlook the aberrant forms. Thus, lead may cause facial and diaphragmatic paralysis, marked sensory loss and even acute ascending paralysis. It may disturb proprioceptive sensibility so that only ataxia is produced. Diphtheric multiple neuritis may produce equally unusual manifestations, and alcohol sometimes produces severe sensory loss without a trace of paralysis. Peripheral neuritis with bilateral facial palsy, on which papers "are appearing at the rate of about one per month," was first described by Laurens in 1869, and many variations are observed in this syndrome. The neuritic symptoms in various infections of the nervous system, including encephalitis, may occur just as local tetanus may be the one manifestation of the general disease. The causal relation of virus infections to polyneuritis still remains to be proved.

FREEMAN, Washington, D. C.

OUTLINE OF CLINICAL PSYCHOANALYSIS. OTTO FENICHEL, Psychoanalyt. Quart. **1**:121 (April) 1932.

This article is the first installment of Otto Fenichel's "Spezielle Neurosenlehre," the authorized translation of which, by Bertram D. Lewin and Gregory Zillboorg, will be first published serially in *The Psychoanalytic Quarterly*, and then will form a monograph to be published separately. The book is designed primarily for the beginner in psychoanalysis, who might wish to consult a "pathology" concerning the illness he happens to be treating, and who might otherwise find it difficult to do so since most of the writings on "analytic pathology" are scattered through the literature. It is also hoped that the nonanalyst will find it helpful in becoming acquainted with the results of psychoanalytic investigation, and that older analytic workers will be able to spare themselves the tedious task of looking up references in the special articles. This installment contains the introduction, devoted to the psychoanalytic concept of the theory of the neuroses, and chapter I, which is devoted to the study of hysteria.

The author begins by stating that psychoanalysis regards the neurosis as a result of a conflict between the instinctual part of the personality and an opposing part, which sets defensive measures into operation and forces a pathologic form on the expression of the instincts. In the beginning psychoanalysis was interested in the instinctual part of the subject, and its chief task was to set this part free from the influence of repression. In doing so it revealed the immense world of the unconscious. This produced other problems for solution, among them, the character of the "repressing" part of the personality which is opposed to the instinctual part. In the "super-ego," the environment inimical to the instincts has created an intrapsychic agency. Accordingly, the ego opposes the instincts because it fears the consequences which it feels might occur if they were gratified.

Two types of external world participate in the formation of the super-ego: the one faced in childhood at the time when the pathologic repressions were being produced; the other from a phylogenetic past which had already been internalized, and which has found organic expression in the organization of the psychic apparatus ("appearance of sexual instinct in two periods," a hereditary tendency to form a super-ego). The relative significance of these two factors is not yet solved. However, psychoanalytic experience indicates that the super-ego arises not from privations which grow out of infantile insufficiency, but from those which parents and educators impose on the child verbally or by their behavior. These educative measures again represent the demands of civilization which are inimical to instinctual gratification, and it is the demands of present-day civilization, with all its contemporary manifestations, which are found in the neurotic patients of today who come for treatment. So far as is known, other civilizations have produced neuroses, but these differed from the neuroses of today because those civilizations demanded different instinctual privations. However, a practical application of a theory of present-day neuroses presupposes in every case the establishment of a definite diagnosis. For practical reasons psychoanalysis divides the neuroses into two large groups. Depending on the clinical attitude of the patient, one deals either with "transference neuroses" or with "narcissistic neuroses." Fenichel also thinks that although all cases incline to be mixed cases, for purposes of presentation these larger groups can be further subdivided under the types he is discussing in this book.

In chapter I conversion hysteria is discussed. After a review of the historical development of knowledge of hysteria Fenichel considers certain basic concepts. One is the concept that hysteria is an expression of a conflict between the repressed (sexual) and repressing forces in the patient. The hysterical symptom may represent: (1) an expression of distorted repressed ideas; (2) an expression of the repressing forces; (3) an expression of both tendencies. In hysteria the patient has reached the phallic stage of development, but has been fixated in his early object choice. Therefore, if he becomes disappointed in his sexual life he comforts himself by regression to the phallic stage of libidinal development. This "return of the repressed" is met by new efforts to repress, and symptoms result. There is some disagreement as to the nature of the repressing forces. Freud believes that repression takes place at the mandate of the super-ego which represents what in childhood was the parental commands; i. e., that the repressing forces are of sociologic origin. The English school of analysts tends to regard the repressing forces as of biologic origin. Fenichel inclines to the freudian concept. He points out that in conversion hysteria the content of the Oedipus wishes, the content of the anxiety and even the anxiety itself are unconscious. The day-dreams indulged in by subjects with hysteria are substitutes for repudiated sexual activity and are derived from early Oedipus fantasies. The pathway from these fantasies to day-dreams is by way of masturbation and fantasies of masturbation, because masturbation in childhood serves as an outlet for the sexual wishes of the Oedipus situation, and the anxiety regarding this situation is displaced onto masturbation. Although oral and anal symptoms occur, the subjects do not regress to these levels, for they never abandon the phallic stage of development or the genitalized relation to objects. Such oral or anal symptoms are used only as a distorted expression of genital sexuality. The prerequisite for the development of conversion hysteria is the turning from reality to fantasy and the replacement of real sexual objects by fantasied representations of infantile objects. The mechanism of conversion seems to be that the symptoms are intermittent or permanent cathectic processes appearing in place of inhibited infantile sexual impulses connected with these impulses through unconscious associations. That is, the hysterical pain was a real pain in the situation in which repression took place and the hallucination was a perception. Certain mechanisms are common in hysteria: (1) Somatic compliance, i. e., the conversion symptom selects that part of the body which is a locus minoris resistentiae. (2) Identifications play a large rôle in hysteria; such identifications may be: (*a*) on the basis of a similar etiologic need; (*b*) with a

fortunate rival (usually by exhibiting a similar discomfort as is suffered by the fortunate rival); (*c*) identification not with the rival but with the object of love; (*d*) multiple identifications.

Fenichel points out the great secondary gain from illness which is so marked in hysteria. He then discusses the mechanism of some typical symptoms. In the hysterical seizure the day-dream is converted into motor activity; the *arc de cercle* may be either the use of innervations antagonistic to coitus or a masculine striving; the dream states are closely related to the seizures; the disturbances of vision are the result of a repressed impulse to look or to exhibit; the hemianesthesias are based on the repressing forces and are the negatives of hallucinations; the paralyses are inhibitions of sexualized motor activity, and the globus hystericus is a materialization of a fellatio fantasy. The latter is a common fantasy in hysterical women and may represent: (1) coitus displaced upward; (2) an act of revenge on a man; (3) an impregnation fantasy; (4) an identification with a man.

In conversion hysteria the prognosis is favorable, and it is the type of illness most susceptible to psychoanalytic therapy. If for any reason this cannot be used, suggestion is of value.

PEARSON, Philadelphia.

OBSERVATIONS ON EXOPHTHALMIC GOITRE. W. H. C. ROMANIS, Brit. M. J. **1**:87 (Jan. 21) 1933.

Romanis begins by remarking that exophthalmic goiter is a mysterious disease, of the pathology of which little is known. It is far more common in women than in men, in blonds than in brunettes, and in single women than in married ones. It nearly always causes more enlargement of the right side of the thyroid than of the left. It is more frequent in certain parts of the world than in others. It is rare in patients under 15 and in those over 55. It is more common among school teachers and brain workers than among manual laborers. It tends to produce a type of woman who is volatile, lively and temperamental, the type of woman who is distinctly attractive to the male. The symptoms and physical signs seem to be unquestionably produced by either an altered or a toxic secretion, or possibly by an excessive amount of normal secretion produced in the thyroid gland. There is considerable evidence pointing to the conclusion that an infective causative agent of some sort, possibly intestinal, is the primary etiologic factor. Other ductless glands are involved. It is possible that the exophthalmos is due directly to suprarenal influence. The thymus is nearly always enlarged. It is common to find a connection between this disease and diabetes.

Other conditions of the thyroid gland may be confused with exophthalmic goiter but Romanis remarks: "I do not regard any case as deserving of the name of Graves's disease unless it presents a certain amount of eye change, a rapid pulse, and definite cardiac changes—slight enlargement in the milder types, and considerable dilatation, with fibrillation and alterations in the heart sounds in the more advanced cases. A microscopic examination of the gland should be made to see if the hyperplasia and changes in the epithelium, which the exophthalmic thyroid gland always shows, are present." Cases are distinguished as primary and secondary. In primary exophthalmic goiter the toxic symptoms have been present from the first, and more or less coincide with the appearance of the goiter, while in secondary exophthalmic goiter a goiter may have been present for years before the full range of toxic symptoms comes on. The primary form is usually the more severe. Secondary exophthalmic goiter shows a marked tendency to give rise to auricular fibrillation, and the results of operative treatment in these cases are even better than those in the primary group. It is suggested that in the primary group there is an altered and toxic thyroid secretion, whereas in the secondary exophthalmic goiter there is an excess of normal thyroid secretion.

Clinically, one encounters cases which show a tendency to marked affection of the nervous system, with tremors, jumpiness, excitability and even mental changes. This group tends to show marked exophthalmos and a large, very hard, rounded, prominent goiter. In the more truly cardiac type of case, with severe dilatation and fibrillation, the goiter is usually softer and less definitely prominent;

exophthalmos is less marked, but pigmentary skin changes are often present. The abdominal type of case, with much diarrhea and vomiting, appears to be intermediate between the above two types. A peculiar shininess or glinting of the cornea, which is often noticeable at some distance from the patient, may precede other ocular changes by a considerable period.

Romanis estimates that probably from 25 to 50 per cent of cases of exophthalmic goiter will ultimately result in death if left untreated. A few will undergo spontaneous change. The majority of patients will develop into chronic invalids, liable to die of any slight infection. Treatment by medical means is discouraging. Compound solution of iodine, given in 10 minim (0.6 cc.) doses, nearly always produces a marked improvement, which, however, lasts only for two or three weeks as a rule. Advantage may be taken of this fact in the physical treatment of the patient. The results of roentgen treatment are not impressive. Cures are rare and relapses common. It renders subsequent operative procedure extremely difficult. Radium, on the other hand, does appear to be more useful in specially selected cases. Surgical treatment has always seemed a reasonable procedure, with a mortality that is very slight (2.5 per cent).

The choice of anesthetic is important, chloroform being highly dangerous. Except in the most severe cases, avertin in the rectum, combined with a minimal amount of gas and oxygen, is satisfactory. In very severe cases, a local anesthetic is by far the safest procedure. The amount of gland to be removed is important and, in Romanis' opinion, error is usually the result of removing too little rather than too much thyroid tissue. In the performance of the operation, the parathyroids may be almost completely ignored. Details of operative technic are given.

Most of the fatalities occur within the first three or four days after operation. Subjective feelings of improvement are usually more pronounced than physical signs. It is often a month or more before pronounced improvement in the physical signs sets in. As a rule, after three or four months one finds that a patient who has had an adequate amount of thyroid gland tissue removed feels well, eats well, sleeps well and can do his day's work. On the other hand, in cases with a grossly dilated and fibrillating heart and advanced myocardial degeneration, it is unreasonable to expect that the heart action can be returned to normal. In patients in whom the basal metabolic rate is from 40 to 80 per cent above normal, it is found that after operation these rates fall within a few weeks to amounts varying from normal to +25 per cent.

The author concludes by remarking: "Of the success of surgery in suitable cases of Graves's disease there is, I think, no doubt, but one cannot help feeling conscious that in removing thyroid tissue one is really treating symptoms and not causes, and that the primary cause is something further back and not yet removable."

FERGUSON, Niagara Falls.

FACTORS IN THE DETERMINATION AND INTERPRETATION OF VISUAL ACUITY. JAMES E. LEBENSOHN, Arch. Ophth. **10**:103 (July) 1933.

Many factors are connected with the determination of visual acuity. The one which Lebensohn uses as an introduction to his paper is of outstanding importance. "Tests for visual acuity in general measure the macular function of the light-adapted eye. Though the binocular field of vision extends to 184 degrees, the true macular field does not exceed more than 2 degrees. The factors determining visual acuity in a healthy eye are chiefly refractive error, visual angle, illumination, or rather brightness, contrast and period of exposure. Subordinate factors are irradiation, color, glare, width of pupil, attention and fatigue." In considering illumination it is essential to understand that the perimacular region is more sensitive than the fovea at the lower intensities of illumination. Much has been written relative to rod vision under such conditions, and the opposite—cone vision under the conditions of the high intensities of illumination. It has been assumed that the rods and cones vary in sensibility, and that their thresholds are distributed according to the usual curve of statistical variability.

Contrast also bears an important relationship in the estimation of visual acuity. Lebensohn's satisfactory consideration of this follows: "An object is not visible unless its brightness differs from that of its background. The degree of contrast is expressed by the ratio of the brightness-difference between the object and its background to the brightness of the background. Black print on a white background has a maximum contrast of 94 per cent; the letters in the telephone directory, about 80 per cent. Under favorable conditions, two grays varying by less than 1 millimicron wavelength can be distinguished as separate shades."

The interrelationship between the important variables—brightness, contrast and size—is illustrated by the following data from Luckiesh and Moss: When the brightness is 2.6 millilambers (1 millilamber is approximately the brightness produced by a 1 foot candle on a good white surface), an object 1 minute in size and with a contrast of 100 per cent is at the threshold of visibility. If the contrast is reduced to 75 per cent, the test object may be brought back to visibility by increasing the brightness to 5.8 millilambers, or by increasing the size to 1.1 minutes.

Relations Between Visual Acuity and Visual Efficiency

Snellen Notation	Percentage Visual Efficiency	Snellen Notation	Percentage Visual Efficiency	Snellen Notation	Percentage Visual Efficiency
20/20	100	20/100	48.9	20/280	9.8
20/25	95.6	20/120	40.9	20/300	8.2
20/30	91.4	20/140	34.2	20/340	5.7
20/40	83.6	20/160	28.6	20/380	4.0
20/50	76.5	20/180	23.9	20/400	3.3
20/60	69.9	20/200	20.0	20/500	1.1
20/70	63.8	20/220	16.7	20/600	0.6
20/80	58.5	20/240	14.0	20/800	0.1
20/90	53.4	20/260	11.7		

A discussion of visual efficiency based on visual acuity is properly included in the article. Other factors must be included in a final determination of visual efficiency, such as muscle imbalance, diplopia and the extent of the field of vision, but on the consideration of the central visual acuity alone, the accompanying table expresses adequately the loss a patient sustains through an impairment of this purely macular retinal function.

Further, the table gives one an idea of percentage loss from the standpoint of compensation.

SPAETH, Philadelphia.

MENTAL DISTURBANCES IN DISEASES OF THE BRAIN STEM AND THE AUTOMATIC SYNDROME. ERICH GUTTMANN and K. HERMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:439 (July) 1932.

Guttmann and Hermann report a case of suprasellar tumor, with mental disturbances characterized by anxiety, compulsions and acoustic delusions. The mental symptoms did not disappear with operation, but evaporated slowly within a year. Necropsy showed a tumor lying between the chiasm and maxillary bodies. The mental troubles must be looked on as amentia. Recent contributions have called attention to the diencephalon and mesencephalon and amential psychoses. Schilder and Weismann reported the case of a woman, aged 21, with a craniopharyngeal pouch tumor; the menses had ceased for six months, and she had shown mental symptoms for six weeks; she spoke beside the point and had lapses of memory; she was disoriented and hallucinated; she heard voices; before falling asleep or during the night she saw the forms of men and women, and once she saw a burning house. Necropsy revealed a tumor which had destroyed the region from the chiasm to the anterior perforated space, and which penetrated into the third ventricle. The pituitary gland was intact. In Guttmann and Hermann's case the tumor occupied the infundibular region, reaching up to the anterior commissure and to the fornix. Anteriorly it was bounded by the optic tracts. In 1927, Schilder reported a pituitary tumor with an incomplete bitemporal hemianopia, loss of

erection, akinesis and mental disturbances in which every night before sleep the patient saw worms crawling around on the bed; during the day he realized that his experiences were hallucinatory. In Schilder's first case, drowsiness was a prominent symptom, just as in the case of Guttmann and Hermann.

Similar mental states have been observed in encephalitis. In the acute stages the psychoses are of toxic type, but in the chronic cases Guttmann was able to collect many paranoid trends in reported cases. Schilder reported two cases of encephalitis with mental changes which he thought were due to pathologic changes in the midbrain. The symptoms in the case of one patient consisted of anxiety, a feeling that there were bodies in bed with her and that sexual perversions were being practiced on her.

Another type of psychosis has been reported in the cases of Lhermitte, Lévy and Bogaert. In the latter's case there was softening in the peduncle and red nucleus, reaching anteriorly to the pulvinar and the superior colliculi and posteriorly to the anterior end of the pons. The patient, aged 59, had a sudden bilateral and then unilateral oculomotor paralysis with a unilateral cerebellar hemiplegia; she had hallucinations of animals and colors; there were no disturbances of sleep, and no disorientation occurred. Similar clinical cases have been reported by Lhermitte and Lévy. In a case of Claude and Lhermitte there was a softening in the mesencephalon. The twelve cases reported in the literature showed that a large area between the infundibulum and pons is involved in cases of involvement of the brain stem with mental symptoms.

ALPERS, Philadelphia.

REGULATION OF THE BLOOD BY THE CENTRAL NERVOUS SYSTEM. R. GINZBERG and L. HEILMYER, Arch. f. Psychiat. **97**:719 (Sept.) 1932.

Ginzberg and Heilmeyer investigated the relationship between disturbances in the central nervous system and changes in the blood picture. In this report they restrict themselves to the occurrence of reticulocytes in the blood. The staining method used was one described by Holboll and later modified by Heilmeyer. This method permits a clear demonstration of the reticulocytes and makes it possible to differentiate between the various groups. The authors describe five forms: (1) Nucleated red cells. (2) Cells characterized by the disappearance of the nucleus, leaving a conglomerate of the substantia reticulo-filamentosa. Neither of these types occurs in normal blood. (3) Cells in which this substance arranges itself in a net form. Normally, there are from 6 to 9 of these cells in each 10,000 red cells. (4) Cells in which only threads remain of the network. Normally there are 15 such forms in each 10,000 red cells. (5) Cells in which there are a few isolated remains of the threads. Normally there are from 55 to 59 such cells in each 10,000 red cells. Altogether, in normal blood there should be from 3 to 12 reticulocytes in each 1,000 red cells, all belonging to the last three groups mentioned. When there is an increase in the number of reticulocytes or a shifting toward the left (that is to say, the occurrence of cells belonging in groups 1 and 2) the condition is regarded as abnormal.

Thirty-two observations were made in thirty cases. In most the blood was studied on several occasions following the withdrawal of cerebrospinal fluid. In some the reticulocyte count was normal both as to number and types. In others there was a change either in number or in form, or in both. No relationship was found between any special type of disease of the central nervous system and changes in the reticulocyte picture. Furthermore, there was no relationship between the amount of fluid removed, the pressure of the cerebrospinal fluid or the blood pressure. In all cases the rest of the blood picture did not seem to bear any relationship to the reticulocyte count. In their positive findings the authors restrict themselves to the fact that abnormalities in the reticulocyte picture were found only in cases of disturbances of the central nervous system in which there existed hydrocephalus, regardless of its cause or of its association with any particular disease process. There also seemed to be a definite relationship between the probable meningeal permeability and the occurrence of abnormalities in the reticulocytes. Although the authors themselves did not undertake determinations

of the permeability, they found that in diseases that are usually associated with increased permeability there was also an increase of the reticulocyte count and an occurrence of abnormal types of reticulocytes, whereas in diseases that are associated with a decreased permeability the opposite occurred.

MALAMUD, Iowa City.

ACTION OF BARBITURIC ACID COMPOUNDS. A. M. MEERLOO, J. Ment. Sc. **79**:337, 1933.

Meerloo reviews the work that has been done by the Dutch group of psychiatrists in the treatment for psychoses with various compounds of barbituric acid. Treatment with barbital originated in the theory that a long-continued sleep and relaxation of the patient would facilitate contact between the patient and the psychotherapeutist which was impossible when the patient was restless, excited and having hallucinations. The spectacular work of Kläsi showed that beneficial therapeutic effects were obtained without the patient going into a profound stupor and without the interference of the psychotherapeutist. The subject is still poorly understood. There are no objective tests that would explain the action of these compounds in cases of psychoses, nor is there an explanation for the extreme variation in the susceptibility of the patient to these drugs. Meerloo asks himself first, what elective actions the drugs have on the central nervous system, and what type of constitutional reaction these drugs evoke. In reviewing his work with 500 cases, he states that in the last 350 no deaths occurred. In 179 cases in which treatment was given in the years 1927 and 1928, 20 per cent of the patients showed definite improvement. He stresses the fact that the most effective compounds are not known; each worker uses his own compounds and claims good results. It is not known what psychotic conditions benefit most with this treatment. Numerically speaking, the greatest success has been achieved with the manic-depressive psychoses. Acute cases respond better than chronic cases. Success comes unexpectedly and cannot be forecast. There are no objective indications as to when the treatment should begin or stop. The length of the treatment varies from eight days to eight weeks. The dangers during the course of treatment are collapse, high fever and anuria. The greater the care exercised, the less striking are the results. One must watch for occasional induction of convulsive states by the administration of the drug. Meerloo believes that the drug acts on the brain stem rather than on the cortex. This belief is based on the fact that anuria and bulbar symptoms develop, as well as on the fact that pathologic material studied by Hage and Spielmeyer showed hyperemias and hemorrhages in the brain stem after poisoning with sodium barbital. The author uses his own compounds of barbituric acid, to which he adds antipyretic substances such as cinchophen and strophanthin. Two cubic centimeters of this mixture is given by mouth twice a day. The method has been used in 44 cases since February, 1931; excellent results were obtained with small as well as with large doses. Meerloo believes that the subject is poorly understood and recommends more research into the problem.

KASANIN, Howard, R. I.

THE SUBNORMAL CHILD—SEVENTEEN YEARS AFTER. RUTH E. FAIRBANK, Ment. Hyg. **17**:177 (April) 1933.

A group of 122 subnormal children, studied in 1914, was reviewed socially and psychologically in 1931. Campbell, reporting the original survey of this group in the first issue of *Mental Hygiene* (January, 1917), divided them into three groups; 12 per cent were seriously handicapped mentally, many being unable to read or write. It was anticipated that this group would add to the ranks of the vagrant, the immoral and the delinquent. The second group, 53 per cent of the children under survey, was definitely subnormal, although the children were less defective than those of the first class. These, it was predicted, would be found drifting along the lowest social levels. The remaining 45 per cent were

borderline or high grade defectives, whose somewhat higher intellectual level was presumably a liability to society, by virtue of its delinquency-breeding possibilities. Of these subnormal children, the 122 available for analysis in 1931 consisted of 72 boys and 50 girls. All but 2 of the latter were married. There were 5 cases of illegitimate motherhood among the girls, and 5 of prostitution.

Of the 122 subjects, only 30 had appealed to social welfare agencies in the last seventeen years. Three fourths of the persons were financially independent—this in spite of the economic depression. Most of the boys in the 1917 survey entered the trades and humbler occupations. One of the children in this subnormal group grew up to become a prohibition agent. There was surprisingly little alcoholism among the children of alcoholic parents. Eleven per cent of the entire group had records of more than one court appearance, and 25 per cent of at least one appearance before the juvenile or upper court. The adults with the bad court records, however, were not necessarily the children who had been delinquent as juveniles. Most of the court cases were from the less retarded groups, justifying Dr. Campbell's prediction. Marriage apparently proved to be a stabilizing factor, both economically and emotionally.

Forty of the subjects were retested seventeen years after the original psychometric study. The scores varied little from the original findings; half of the 40 subjects had a mental age of less than 12 at the time of retesting, while the remaining half fell in the dull normal group. Their children, however, placed in somewhat higher psychologic categories.

A corresponding survey was made of a control group of children of normal intelligence, attending the same school. In this group marriage took place at a much later age; delinquency and crime were much less, and the vocational status was much higher. The paper is rich in statistical citation and should be read in full for an adequate understanding of the interpretation of this survey.

DAVIDSON, Newark, N. J.

OLFACTORY DISTURBANCES IN PATIENTS WITH CRANIOCEREBRAL TRAUMATISM. J. HELMSMOORTEL, JR., R. NYSSEN and R. THIENPONT, Rev. d'oto-neuro-ophth. **11**:489 (July-Aug.) 1933.

Anosmia and hyposmia are caused by obstruction, lesions of the olfactory mucosa, lesions of the olfactory nerve centers or pathways and hysteria. Except in the rare cases of anosmia from serious traumatism of the nasal skeleton or of the sensory epithelium and direct injury to the pathways or centers, anosmia from mechanical causes is almost always caused by cranial traumatism. According to Laemmle, traumatisms of the anterior fossa cause olfactory difficulties more often than those of other regions of the skull. Woelk emphasized the importance of anosmia among certain workers: cooks, merchants of wine, tea, coffee and tobacco and perfumers.

The authors studied the sense of smell in forty-three cases of craniocerebral traumatism. Examination should be made soon after the accident and repeated several times, since in some cases there is regression or modification of the anosmia. Two groups of odorous substances were used, the first purely odorant and the second with a concomitant extra-olfactory action, affecting the trigeminus and the sense of taste. The use of the latter group aids in determining malingering and hysteria. The respiratory and plethysmographic reactions were observed when possible in those with marked subjective olfactory troubles. An estimate was made of the degree of anosmia by observing the time elapsing between the presentation and the perception of the odors. Of the forty-three cases, there were six of complete and lasting anosmia, two of complete anosmia evolving into hyposmia, seven of partial or variable anosmia, three of olfactory disturbances caused, probably, by mental torpor, one of simulated anosmia and two of anosmia due to previously existing nasal lesions. Of the twenty-three remaining cases, probably some had presented temporary anosmia which had disappeared before the examination. In five of the six cases of complete anosmia, a fracture was present which in three

involved the ethmoid bone. Of the nine cases of less severe olfactory disturbance, only one presented a fracture. Among the twenty-three osmatic cases, none presented evidence of fracture of the ethmoid bone. Olfactory disturbances from blows on the occiput were found only once. In two cases in which the olfactory troubles definitely regressed, a reduction of the period of latency was observed at each examination. The discovery of two cases of complete anosmia caused by preexisting nasal lesions emphasizes the necessity of rhinologic and roentgenologic examination of the naso-ethmoid region. DENNIS, Colorado Springs, Colo.

ENCEPHALITIS, POLIOENCEPHALITIS AND VACCINAL ENCEPHALITIS IN CHILDREN. C. PAGET LAPAGE, Brit. M. J. **1**:811 (May 13) 1933.

Encephalitis may follow vaccinia, variola, varicella, zoster, epidemic encephalitis and poliomyelitis, all of which are virus diseases. It may, in addition, follow pertussis, mumps, rubella and influenza, all diseases likely to be of virus origin. The pathology of encephalitis is that of widespread and marked degeneration of ganglion cells, with vacuolation, neuronophagia, areas of hyperemia and small hemorrhages. All virus diseases show a distinct tendency to a selective action on certain areas of the brain.

Vaccinal encephalitis is of interest and importance. In England the rate is 1 case in about 33,000 vaccinations, and 1 death in 60,000. The pathologic changes are those of a severe disseminated encephalomyelitis. From 30 to 40 per cent of patients die from three to ten days after the onset. The symptoms usually begin from ten to thirteen days after vaccination. The age of onset is usually between 3 and 13 years. This indicates that vaccination should take place in infancy and at the earliest age possible. The most successful treatment is the injection of serum from an immune person, intrathecally, if possible.

Polioencephalitis is an inflammation of the gray matter, due usually to a specific virus which reaches the brain probably by way of the perineural lymphatics from the nose and throat, or from the gastro-intestinal tract, or even from the trachea and bronchi. It tends to occur in the dry, dusty autumn. In children who are having an attack the disease is infectious, but not strongly so. It is the author's opinion that in some of the children who have had infantile paralysis the disease may become periodically infective. Other carriers have been thought to be the stable fly and domestic animals. The virus can be attacked and its spread prevented by the injection intrathecally and intravenously of from 20 to 50 cc. of convalescent serum. Rest in these cases is also of great importance.

Epidemic encephalitis is discussed briefly. The author believes that there is evidence that more than one virus might cause epidemic encephalitis.

Exanthematous encephalitis occurs especially in measles. It may be severe in its effect at first, but tends to clear up and leave no bad effects. It is suggested that this form of encephalitis may not be a true inflammatory process, but rather a toxic condition. Acute toxic encephalitis may also occur in diphtheria.

FERGUSON, Niagara Falls, N. Y.

HEMATOMYELIA TUBULARIS SYMMETRICA. G. C. BOLTEN, Monatschr. f. Psychiat. u. Neurol. **78**:274 (April) 1931.

The author reports seven cases of hematomyelia tubularis symmetrica and discusses the literature on this subject. Tubular hemorrhages of the spinal cord are generally caused by traumas that produce sudden flexion or extension of the vertebral column, as a result of which a small blood vessel is torn. Such hemorrhages are observed most frequently in the cervical and lumbar regions. They are almost always situated in the gray matter, which is more richly supplied with blood vessels and is less resistant than the white matter. Since the extravasated blood is prevented from spreading laterally by the dense fiber tracts, it usually extends longitudinally in the gray matter and across the gray commissure to the

opposite side, where it tends to spread in the same manner. Spontaneous hemorrhages are rare. They are encountered more frequently in hemophilia and other diseases of the blood than in arteriosclerosis, which seldom involves the spinal vessels. According to some authors, spontaneous hematomyelia occasionally owes its origin to the rupture of a small congenital aneurysm.

As a rule the symptoms develop suddenly. There are severe paresthesias, and flaccid paralysis of the arms or legs or of all four extremities occurs almost immediately. The bladder and rectum are generally involved. Although a dissociated disturbance of sensation is not uncommon, sensory impairment is usually not a prominent feature. The tendon reflexes are absent. If the plantar reflex is preserved it is apt to be extensor in type. Muscular atrophy takes place later and in most cases is severe. When the hemorrhage occurs in the cervical segments oculopupillary symptoms may be observed. As a rule, the skin and nails show trophic changes. High cervical lesions may lead to sudden death from respiratory failure, but hemorrhages in that region are rare. Unless complications such as pneumonia, sepsis from decubital ulcers or cystitis arise, gradual improvement is to be expected within from three to five months. There is frequently a remarkable restoration of function. In Bolten's cases, however, complete recovery did not occur.

ROTHSCHILD, Foxborough, Mass.

THE DEVELOPMENT OF THE CEREBELLUM IN AMBLYSTOMA. O. LARSELL, J. Comp. Neurol. **54**:357 (April) 1932.

The development of the cerebellum in Amblystoma is traced from the time when the first cells which can be definitely ascribed to the cerebellar anlage appear, through the various physiologic stages in the growth of the larva to the stage when the organ attains the essentially adult characteristics. No attempt has been made as yet to correlate anatomic findings with the functional capacity of the cerebellum in the larvae of the various stages described.

The first indication of cerebellum consists of a group of modified Rohon-Beard cells in the alar plate just caudal to the cephalic flexure on either side. The group develops into a common anlage for corpus cerebelli and medial part of the auricular lobe, but the latter does not become distinct from the cerebellar body until four days after the early swimming stage. Large and small cells may be distinguished quite early. Fibers from the large cerebellar cells and from similar cells in the superior V region cross dorsomedially to form the cerebellar commissure, which appears as a definite bundle of fibers during the first day of early swimming. Finer fibers from small cells in the auricles cross as the lateral commissure, which is formed later than the cerebellar commissure and lies caudal to it. The lateral commissure connects the vestibular and lateral-line-serving auricles, while the cerebellar commissure connects the trigeminal regions, primarily. Cells migrate medially along these two commissures to form the adult cerebellum. The acousticolateral area is recognizable at the stage of two and one-half days after early swimming and the auricular lobe is also foreshadowed at this stage. The rostral part of the acousticolateral area fuses with the common anlage of the corpus cerebelli and auricle to form the definite auricular lobe. This is relatively very large in midlarval stages but becomes reduced in proportionate size later. The auricular lobe is a transitional zone, structurally and functionally, between the acousticolateral area and the body of the cerebellum. The fiber tracts are described and the histogenesis of cells is followed.

ADDISON, Philadelphia.

SYPHILIS AND THYROID DISEASE WITH SPECIAL REFERENCE TO HYPERTHYROIDISM. E. W. NETHERTON, Am. J. Syph. **16**:479 (Oct.) 1932.

Syphilis is not an important factor in diseases of the thyroid gland; occasionally one encounters congenital syphilis which, by destruction of the glandular epithelium, has produced cretinism. Gumma of the thyroid gland is rare, only one case appearing in Netherton's series. Late syphilis practically never involves the thyroid gland. In reviewing the literature, Netherton was impressed

with the carelessness with which a diagnosis of exophthalmic goiter was often made; frequently, the disappearance of thyroid symptoms following antisyphilitic therapy was accepted as evidence of the causal relationship between the two conditions. This Netherton condemns as illogical and unscientific. In all, sixty-two cases are presented. Seventy-two per cent of the patients had hyperthyroidism, while 25 per cent had adenoma of a nontoxic type. In the former group, one-third had syphilitic involvement of the central nervous system, while in the other two-thirds the central nervous system had apparently escaped, other organs showing the effects of the syphilis. In instances in which hyperthyroidism and syphilis were combined, the condition responded best to surgical intervention, with a course of antisyphilitic therapy following rather than preceding the operation. Convalescence was not prolonged. It is Netherton's belief that in most cases of alleged syphilitic hyperthyroidism, the syphilis had produced an effect on the vegetative nervous system which in turn had resulted in the tachycardia and sweating on which the diagnosis of thyroid disease was made.

DAVIDSON, Newark, N. J.

PLANTAR TENDON REFLEXES. S. M. WEINGROW, Bull. Neurol. Inst., New York **2**:312 (July) 1932.

The author reviews briefly the literature on plantar tendon reflexes, illustrating the differences of opinion that exist concerning the physiology and clinical interpretations. He considers that these differences are due to the fact that, while the motor responses of the reflexes are few, the afferent pathways are numerous, and the great variation in the method and place of stimulation has led to confusion in interpretation. The tendon reflexes of the sole of the foot were studied by a method of marking, which located the tendon stimulation points of the various muscles; these were stimulated by tapping, which produces a muscle stretch and reflex motor response. Seventy-six normal subjects, ranging in age from 4 months to 67 years, were studied. The Rossolimo sign, considered indicative of disease of the pyramidal tract, was found in normal subjects with hyperactive reflexes. Plantar tendon reflexes were weak or not elicited only in those who suffered from arthritis, flatfoot or other orthopedic disturbances. Individual studies in subjects with involvement of the spinal cord, brain and peripheral nerves showing absence of the plantar tendon reflexes are reported, and the method of elicitation is outlined. Examination of these reflexes is considered of clinical importance because they arise from motor cells in the fourth and fifth lumbar and first and second sacral segments, whereas the achilles reflex response arises from the first and second sacral alone.

KUBITSCHEK, St. Louis.

PROLONGED NARCOSIS AS THERAPY IN THE PSYCHOSES. HAROLD PALMER and ALFRED PAINE, Am. J. Psychiat. **12**:1 (July) 1932.

To produce deep unconsciousness approaching so far as possible normal profound sleep, Palmer and Paine employed two technics: (1) that with phenobarbital and (2) that with sodium amytal. The first consisted of the administration of phenobarbital and sodium barbital, followed by a course of chills and fever induced by typhoid vaccine. The preparations of barbital were given both orally and intravenously in a dosage sufficient to produce narcosis for a week or ten days. The second regimen consisted in giving 15 grains (1 Gm.) of sodium amytal in a 5 per cent solution intravenously, at a rate of injection of 1 cc. a minute. The injection is given daily at 9 a. m., and the same preparation is administered orally in tablet form during the day in order to assure persistence of the narcosis. Twice a day the patient is permitted to remain awake for feeding and evacuation. The intake of fluid is maintained at 3 liters daily and the amount of food at 3,000 calories daily. Narcosis was continued for from seven to ten days.

Of the schizophrenic patients, 33 per cent showed recovery or permanent improvement, while in the manic-depressive group 75 per cent could be discharged cured or permanently improved. The highest rate of recovery occurred among those subjected to the phenobarbital regimen. This was the most debilitating and most toxic program, and apparently owed its efficacy to this fact. No deaths occurred, and in no case did the drug fail to produce adequate narcosis.

DAVIDSON, Newark, N. J.

THE INDIVIDUAL FACTOR IN MANIC REACTIONS. P. R. VESSIE, J. Nerv. & Ment. Dis. **75**:113 (Feb.) 1932.

The author stresses the fact that a study of the cyclothymiac mood swings of the manic-depressive psychosis does not support a purely hereditary interpretation, and he attempts to throw into relief the individual variation and manifestation of seven manic-depressive patients. The cases are described graphically and in detail, without attempts at interpretation. At least one parent of each patient showed melancholic or manic mood states. In the patient's personality, oversensitiveness, irritability, narcissism and flexibility of mood were outstanding features. One patient seemed to have the power of consciously starting a manic attack of combativeness, irritability or erotism, but in the depressed phase had bizarre somatic delusions. In the second patient dreams formed a means of pushing distressing memories *hors de combat*. Personal failure in a third patient exaggerated the preexisting cyclothymiac tendency to a pathologic degree. A fourth patient found great sexual gratification, normally thwarted, in her manic swings. Another patient in a depression, with evidence of thyroid exhaustion, improved with a rapid increase of the basal metabolic rate; before regaining normality she went through a period of manic ecstasy. The sixth patient showed a special intolerance for sodium bromide, which seemed to stimulate the exalted phase. The last patient, depressed after a postinfluenzal encephalitis, passed from a state of confusion and perplexity into a hypomanic elated state. Endocrine, metabolic and autonomic disorders were observed, particularly in the depressive phase preceding the manic reactions.

HART, Greenwich, Conn.

PSYCHIATRY AND THE CRIMINAL. FREDERIC H. LEAVITT, Am. J. Psychiat. **12**: 541 (Nov.) 1932.

Correction of the criminal urge during the formative years of childhood is essential to further progress in prophylactic criminology. To this end it is essential that juvenile courts be separated from ordinary courts, that places for the detention of children be in quarters removed from the jails used for the adult population, and that the juvenile courts be assisted by adequately manned psychiatric clinics. In the field of sociologic improvement, Leavitt suggests the eradication of slums, stressing their importance as a breeding place for crime. He is inclined to credit the relative absence of congested areas in European cities with their excellent record for obeying the law. The reform school, by whatever name it is called, has failed to reform its inmates and is scarcely more than a prison; it offers little hope for further preventive work. Probation, on the other hand, is a more fruitful field, although a more highly trained and better paid personnel will be essential before probation can work efficiently. In the field of adult criminology several suggestions are offered; a procedure like that followed under the Brigg's law of Massachusetts, whereby all persons indicted for felonies are placed under psychiatric observation before the trial, is recommended. Confidence in the sincerity of the psychiatrist will be promoted if the experts who advise the counsel refrain from taking the stand, while those who do testify avoid the counsel table. The closer association between schools and child guidance clinics is also urged.

DAVIDSON, Newark, N. J.

REPORT OF A CASE OF TRAUMATIC MYELODELESIS. E. KATZENSTEIN, Nervenarzt **5**:192 (April 15) 1932.

Katzenstein reports a case in which signs and symptoms of a progressive lesion of the cervical cord appeared subsequent to a fall on the back of the head and neck. Immediately after recovering consciousness, the patient, a man, aged 26, became aware of weakness in the extensor muscles of the neck. This weakness increased, and in the following months the muscles of the shoulders and arms became involved. Muscular atrophy was first noticed nine months after the accident, and when the author first saw the patient eight months after this, definite fibrillary twitchings were observed. As the weakness and atrophy continued to progress, evidence of invasion of the bulbar centers and, to a lesser degree, of the pyramidal tracts appeared. Hyperalgesia and a slight impairment of temperature sense were noted over an area extending from the second cervical to the sixth dorsal dermatones. When the patient was last seen four and one-quarter years after the accident, it was evident that progression had been in abeyance for the preceding two years.

The author expresses the view that an ascending and descending gliosis, possibly accompanied by cystic degeneration, was superimposed on the original traumatic lesion. Traumatic myelodelesis, a term introduced by Kienböck, differs from syringomyelia in that progression is limited in the former condition. The literature relative to the traumatic origin of progressive muscular atrophy and syringomyelia is reviewed briefly.

DANIELS, Denver.

OF THE WORDS "CHARACTER" AND "PERSONALITY." WILLIAM MCDOUGALL, Character and Personality **1**:3 (Sept.) 1932.

This is the first article in the first issue of a new journal the name of which is analyzed in the opening paper. The German edition of the periodical bears the title *Charakter*. It is significant that this one word expresses both "character" and "personality" in the English designation. The term "character" in English is vaguely and uncertainly defined; popularly it refers to the single distinctive property of a person or thing in contrast to the German word, which embraces the sum total of an individual's features. Furthermore, in its limited English sense, character is associated with the qualities of volition, decisiveness and consistency. Psychologists have difficulty in defining the word and seem unable to fit it into the general psychic scheme. Indeed it has been suggested that one should recognize a new science of character to take its place beside psychology, the science of ideas. Character is part of the personality, but developed gradually through social intercourse. It must be distinguished from temperament, which is a more or less temporary quality, a sort of transient inner environment in which character dwells. Drunkenness, for example, modifies temperament without changing character. Nor are these two qualities the whole of personality; intelligence, temper and disposition must be added. As each is a heading under which are classified a multitude of complex functions, it is futile to search for a limited number of well defined types of personality.

DAVIDSON, Newark, N. J.

GERMICIDAL EFFECT OF ULTRAVIOLET RAYS ON THE VIRUS OF HERPES. TRYGVE GUNDERSEN, Arch. Ophth. **8**:519 (Oct.) 1932.

Much confusion exists as to the value of ultraviolet rays in the treatment of infections as well as other disorders of the eye. Brilliant results have been described in the neuropathic group of diseases, and particularly in the herpetic group, in which dendritic keratitis is outstanding. These observations have been made only in isolated cases or in small groups of cases such as reported or cited in discussions by Duke-Elder, Bernd, Post, Walker, Gifford, Green, Stock, Peppmuller and others.

Certain groups of cases of herpes were used, wherein the aims were: (1) destruction of the herpes virus in the cornea of an eye after enucleation, (2)

exposure in vitro of the virus of herpes to ultraviolet rays, (3) the production of the effect of previously irradiated serum on subsequently added virus, (4) irradiation of herpes virus through blood serum in a quartz cell, (5) irradiation of herpes virus in saline solution through a glass plate, (6) irradiation of herpes virus in the living rabbit's cornea after different periods of incubation, (7) irradiation of herpes virus in an isolated flake of superficial corneal tissue with epithelium intact and (8) the augmentation of ultraviolet activity by fluorescein. From these experiments the author concluded that the virus of herpes cannot be destroyed in the cornea by exposure to ultraviolet rays, which would be practical to use on the human eye, and that staining of the cornea by aniline dyes does not enhance the germicidal effect of ultraviolet rays on the virus of herpes.

SPAETH, Philadelphia.

OPHTHALMO-ENCEPHALO-MYELOPATHY. S. E. BARRERA, Psychiatric Quart. **6**:421 (July) 1932.

In a woman, aged 27, in whose case a diagnosis of hebephrenic dementia praecox had been made, blurring of vision and inadequacies of motor control began to develop; thirteen months after the first appearance of symptoms, she died of an intercurrent double pneumonia. Autopsy showed diffuse degeneration of the long ascending tracts of the spinal cord and spotty involvement of the optic system, with no evidence of any reactive or inflammatory response on the part of the central nervous system. The disease entity bears certain resemblances to Schilder's disease group, although the age of the patient and the marked spinal involvement remove it from that class in its narrower sense. Because of the limitation of the cord degeneration to the sensory tracts, it is not reasonable to classify it as an acute multiple sclerosis. The cases of so-called "neuro-ophthalmomyelitis" are not properly comparable to this condition, owing to the noticeable inflammatory response found in these instances. Barrera applies the designation "ophthalmo-encephalomyelopathy" to his patient's condition, considering it an intermediate type in the large, diverse group of Schilder's disease, encephalomyelitides and ophthalmoneuromyelitides. The mental symptoms can also be explained on the basis of a pathologic condition of the occipital (visual hallucinations) and frontal (motor phenomena) lobes, although the author is unwilling to commit himself unqualifiedly to the view that the mental symptoms were due to the underlying cerebral degeneration.

DAVIDSON, Newark, N. J.

RETROBULBAR NEURITIS DUE TO THALLIUM POISONING FROM DEPILATORY CREAM: REPORT OF THREE CASES. WILLIAM MAHONEY, J. A. M. A. **98**:618 (Feb. 20) 1932.

Mahoney reports the case histories of three patients who were referred to the neurosurgical service of the Peter Bent Brigham Hospital by ophthalmologists because of failing vision and suspected chiasmal michief. Each of these patients gave a history of the use of a proprietary depilatory, Koremlu Cream, which has long since been brought to the attention of the Bureau of Investigation of the American Medical Association, and on which the bureau reported with regard to its constituents, all this because of the appearance of peripheral neuritides in people who had been using this cream. The review indicated that the active principle was thallium and the percentage of the acetate present was 7.18, an unusually bold potency in view of Sabouraud's earlier caution to use it sparingly and in a strength no greater than 1 per cent. In presenting the proprietary cream, the distributors advertise it most attractively, convincingly and with absolute assurance that no harm will follow its use. The author's purpose is to point out the dangers that follow long-continued use of this preparation. The three cases presented were in patients who entered a neurosurgical clinic as "intracranial tumor suspects," and were found to have an advancing retrobulbar neuritis. Their failing vision has been checked and improvement made by discontinuance of the depilatory, which, therefore, is the most probable source of the disorder.

EDITOR'S ABSTRACT.

THE FUNCTIONING OF MEMORY AND THE METHODS OF MATHEMATICAL PRODIGIES. BELA SANDOR, Character & Personality **1**:70 (Sept.) 1932.

Sandor, having examined Finkelstein, the Polish calculating expert, reports that he did not show any evidence of mathematical skill until he was 22 years old; he had always had a lively interest in numbers—almost a sentimental attachment to certain figure groups; curiously he had no grasp of the deeper philosophic aspects of mathematics, devoting himself to calculating skill and feats of memory. His general intelligence was only average. Some prodigies (like Inaudi) have a predominantly acoustic-motor disposition and work best when subject matter is read aloud; this was not the case with Finkelstein, however, who had a visual type of imagination.

Finkelstein memorized rows of figures in groups of three digits, thus accumulating partial sums; the further manipulation of these three digit units was often associated with motor acts of almost compulsive force. Sandor lists the chief requisites for this type of calculating ability as memory, speed in manipulation of numbers, orientation among the figures and power of intensive concentration. It is to be regretted, the author concludes, that the lasting, one-sided preoccupation of the mind with this more or less rudimentary function results in a deterioration of deductive reasoning powers, the memory, as it were, ceasing to be an instrument of creative activity and becoming an end in itself.

DAVIDSON, Newark, N. J.

CONVULSIONS IN CHILDHOOD. M. G. PETERMAN, J. A. M. A. **99**:546 (Aug. 13) 1932.

Peterman reports the results of a study of 419 cases of convulsions in children. A diagnosis was established in 93.3 per cent. The study includes a complete history, a careful physical examination, including neurologic studies, a blood count, a Wassermann test of the blood and microprecipitation tests, urinalysis, examination of the spinal fluid (except in spasmophilia), examination of the fundi, x-ray pictures of the skull and examinations of the stools. In the past three years the author has made encephalograms in doubtful cases. The results reveal that certain diseases peculiar to childhood are the direct causes of most of the convulsions. While some children may be said to be particularly susceptible to the convulsive state, this study indicates that there is usually a physical basis for this susceptibility (spasmophilia or epilepsy) which is amenable to treatment. Every convulsion produces a certain amount of cerebral injury and therefore lowers the threshold for subsequent seizures. Every convulsion demands a careful study and effort to prevent a recurrence. It is extremely unfortunate that there are still physicians who consider convulsions a necessary evil of childhood and advise parents that the child will "outgrow" the tendency. The author presents a practical classification of convulsions in childhood based on the age of the patient.

EDITOR'S ABSTRACT.

THE EFFECT OF RETARDED BODY GROWTH ON THE RESPONSE OF SPINAL GANGLIA SUBJECTED TO EXCESSIVE PERIPHERAL LOADING. R. L. CARPENTER and ELSIE CLARK CARPENTER, J. Exper. Zool. **64**:187 (Nov. 5) 1932.

Homoplastic heterotopic transplantations of differentiated forelimbs were performed on larvae of Amblystoma punctatum ranging from 21 to 30 mm. in length. The larvae were then divided into three groups, one being maximally fed, one moderately fed and the other receiving only enough food for subsistence. An expected hyperplasia in the spinal ganglia supplying the grafted limbs, based on the measured amount of increase in skin area and muscle volume, was computed for several cases. In the larvae which showed an appreciable amount of body growth during the time that the ganglia were subjected to peripheral overloading, the actual hyperplasia (calculated from cell counts of the ganglia) was in excess of that expected. In the larvae which underwent very little growth, or which

decreased in body length, the actual hyperplasia was less than that expected. It is concluded that in an animal lacking sufficient nourishment for normal body growth, spinal ganglia subjected to excessive peripheral overloading are able to respond, by proliferation of additional afferent neurons, only partially or not at all to the stimulus of that overload. The results also suggest that in experiments involving transplantation or excision of a limb, proprioceptive neurons concerned with joint or tendon sensibility may be a factor in the resulting hyperplasia or hypoplasia of the spinal ganglia.

WYMAN, Boston.

MEASUREMENT OF MENTAL DETERIORATION IN DEMENTIA PRAECOX. RUDOLPH SCHWARZ, Am. J. Psychiat. **12**:555 (Nov.) 1932.

Schwarz, using the Babcock test on 110 schizophrenic patients, found it a useful measure of deterioration. The test is based on the assumption that in mental deterioration the vocabulary of the patient is less affected than other intellectual functions. It is justified theoretically by the priority of the development of language in the normal infant, and empirically by the success of the procedure in experiments such as the one here reported. To perform the test it is necessary to obtain the mental age by ordinary psychometric tests and the vocabulary mental age by a special word-recognition test. Presumably the Binet-Simon technic is used, although the author does not name the type of examination employed. The general mental age is subtracted from the mental age judged according to vocabulary and the plus or minus result is designated as the index of efficiency. In normal persons this index is close to zero. In 110 schizophrenic patients Schwarz found a minus index in 104 cases and a plus index in 6; all of the latter patients were well preserved and to the casual observer would display little evidence of psychosis. The average efficiency index of the 110 patients was $-3\frac{1}{2}$. In some of the more deteriorated schizophrenic patients, an index of -7 or -8 was found. The test, Schwarz believes, may be profitably used as an auxiliary criterion for the differentiation of the benign and malignant mental processes.

DAVIDSON, Newark, N. J.

THE STROKE IN HIGH ARTERIAL PRESSURE. H. O. GUNEWARDENE, Brit. M. J. **1**:180 (Jan. 30) 1932.

The author calls attention to the fact that although much prominence has been given to the study of high arterial blood pressures, much still remains hazy, unknown and unexplained. The etiology is but vaguely understood, while therapy has been for the most part symptomatic. It would seem that too little attention in the past has been paid to the early stages, and it is with this aspect of the problem that the present study is concerned. Some of the most important findings are: 1. Cerebral hemorrhage does not seem to occur with diastolic blood pressures under 115 (whatever may be the systolic pressure), and prognosis can be based on this observation. 2. Cerebral hemorrhage occurs most frequently in people working in defiance of an already existing increased pressure and without taking any account of this abnormality. 3. Any kind of paresis or paralysis is rare in cases in which the diastolic pressure is under 115 at the time of the stroke. Strokes at this pressure are rarely fatal or permanent. The former occurs in patients with thickened vessels or other disease; the latter in an unfortunate few, or in those in whom the causative factor is other than hypertension. 4. Cerebral hemorrhage seems to occur most frequently in cases of hypertension which do not show either marked cardiac enlargement or symptoms, and rarely in cases in which there are signs both of considerable cardiac enlargement and of cardiac failure.

FERGUSON, Niagara, Falls, N. Y.

THE PROGNOSTIC SIGNIFICANCE OF THE WASSERMANN REACTION IN NEUROSYPHILIS. BERNHARD DATTNER, Jahrb. f. Psychiat. u. Neurol. **48**:112, 1932.

Extensive systematic examinations of the blood and spinal fluid were made by the author in patients suffering from neurosyphilis who have been under his

observation for many years. He found that in some cases with definite clinical improvement and a remission lasting a decade, which in his experience excludes cases of this type from the danger zone of a dementia paralytica recidive, the Wassermann reaction was still positive in the blood. In cases in which the blood serum was negative and remained so for several years the reaction did not become negative immediately after the conclusion of the treatment, but it took a long time, in some instances several years, to achieve that result. The investigation further showed that following effectual treatment, as manifested by an excellent clinical result, the Wassermann reaction in the spinal fluid did not become negative until five or six years after the treatment, whereas the other reactions in the fluid, especially the cellular content, became normal long before the Wassermann reaction became negative. In the cases in which the number of cells remained high after treatment the other reactions in the spinal fluid also remained pathologic. Dattner concludes, therefore, that by itself the Wassermann reaction is of no value as a criterion as to the ultimate prognosis of a patient suffering from neurosyphilis.

KESCHNER, New York.

HEREDITARY CEREBELLAR ATAXIA. L. RIMBAUD, H. VIALLEFONT and A. BALMÈS, Rev. d'oto-neuro-opht. **10**:697 (Nov.) 1932.

The case of a woman, aged 33, whose symptoms began eleven years previously with failing vision and disturbed gait, is reported. A brother, mother, uncle, aunt and two great-aunts had been similarly afflicted. Station and locomotion were greatly disturbed, and the reflexes were exaggerated, with clonus of the feet and patellae. Hypermetria, deviation to the right in the test of the extended arms, trembling of the head, scoliosis and scanning speech were present. Movements of the eyes to both sides were limited, vertical movements were abolished, and convergence was almost impossible. Vision was 2/50 in each eye. In both eyes the papillae were pale and the arteries were slender, and there were pigmented deposits near the macula of the right eye. Pupillary reflexes were normal, and there was no nystagmus. Vestibular examination showed a slightly positive Romberg sign, no nystagmus after douching of the ears and no vertigo from the galvanic test. The results of laboratory examinations were negative. No previous illness that might have caused the condition was discovered. The complete inexcitability of the labyrinths rather than the ophthalmoplegia explains the absence of the nystagmic reaction. Ophthalmoplegia is exceptional in Marie's type of ataxia. Friedreich's ataxia and multiple sclerosis were considered in formulating the diagnosis, but the weight of evidence was in favor of the original diagnosis.

DENNIS, Colorado Springs, Colo.

THE EFFECT OF THE INGESTION OF A LARGE AMOUNT OF FAT AND OF A BALANCED MEAL ON THE BLOOD LIPIDS OF NORMAL MAN. EVELYN B. MAN and EDWIN F. GILDEA, J. Biol. Chem. **99**:61 (Dec.) 1932.

Using their modification of Stoddard and Drury's volumetric method for the measurement of serum fatty acids, presented in a previous paper in the same volume, the authors studied the normal range of serum fatty acids in man in the post-absorptive state. The ingestion of from 3.5 to 4 Gm. of fat per kilogram of body weight by nine normal men and women produced a marked rise in serum fatty acids and a moderate increase in serum phospholipids. The average rise in serum fatty acids was 62 per cent, the maximum 133 per cent and the minimum 34 per cent above the fasting level. The average rise in phospholipids, determined as lipid phosphorus, was 18 per cent—maximum 28 and minimum 5 per cent. In six subjects the apex of the rise was reached in four hours and in three it came after six hours. The ingestion of a balanced meal containing at least 0.6 Gm. of fat per kilogram and with carbohydrate plus protein slightly exceeding the weight of the fat, produced an average rise of 21 per cent and a maximum increase of 40 per cent three hours after the ingestion of the meal. The phospholipids showed

only a slight increase. The ingestion of other foods with fat did not prevent the rise in serum fatty acids, as has been claimed by some workers.

DAILEY, Boston.

THE PHENOMENA OF "RESSENTIMENT" IN THE DREAM. E. KRETSCHMER, Arch. f. Psychiat. **96**:227 (March) 1932.

This paper represents a report made by Kretschmer at the General Medical Congress for Psychotherapy on May 14, 1931. In it he stresses the importance of dream analysis and its utilization in the treatment of certain types of mental disease. He deals particularly with the neuroses that develop in persons in whom a gap between abilities and ambitions lead to the development of *"Ressentiment"* and subsequent production of symptoms that tend to cover the actual issue. He discusses a series of patients in whom this process led to the development of neuroses, in which the symptoms could be understood only on the basis of dream analysis. In these dreams the author was able to see the actual problem under which the patient was laboring, and, what is more important, to have the patient gain an understanding of these problems. For the sake of gaining further knowledge of these relationships it is important that unbiased scientific investigation in a large number of patients be undertaken. Such things as symbols in dreams and their relationship to emotional difficulties can be definitely understood only on the basis of repeated scientifically valid proof that these relationships actually exist and are not merely a figment of the physician's imagination.

MALAMUD, Iowa City.

NASAL DISCHARGE OF CEREBROSPINAL FLUID, LASTING FOR YEARS. F. J. COLLET, Rev. d'oto-neuro-opht. **10**:660 (Nov.) 1932.

This contribution is a detailed report of the case of a man who, following a fall on the head, had a flow of cerebrospinal fluid from the nose that lasted nearly three years. The flow was small in quantity and more or less intermittent, and was accompanied by headaches, epileptic attacks and anosmia. It was assumed that the patient had suffered a fracture of the cribriform plate, although it is known that fracture of the petrous bone without tympanal rupture can cause a leakage of the fluid through the eustachian tube and thence through the nose. Anosmia may be caused by tearing of the meninges and compression of the olfactory nerves by the consequent hemorrhage or by tearing of the olfactory filaments themselves. Anosmia is a frequent complication of cranial traumatism, especially when the force is applied to the occiput or forehead. It is noteworthy that no serious consequences have resulted in this case from the prolonged flow. Of sixty patients with cranial fractures accompanied by nasal loss of cerebrospinal fluid reported by Schoenbauer and Brunner, eighteen died. This does not take into account those who may die from meningitis after the cure is apparently complete.

DENNIS, Colorado Springs, Colo.

CELLULAR PROLIFERATION IN THE SPINAL CORD OF AMBLYSTOMA FOLLOWING TRANSECTION AND REPLANTATION OF VARIOUS EMBRYONIC-CORD SEGMENTS. S. R. DETWILER and B. L. MACLEAN, J. Exper. Zool. **62**:433 (July 5) 1932.

Cellular hyperplasias in various regions of the spinal cord when grafted from one position to another have previously been described in a series of papers. The question has arisen whether or not such cellular responses may have been partially due to injury inflicted during the grafting. Experiments involving two types of injury to the embryonic spinal cord have been made. In the first, a three-segment piece of cord at three different levels was severed from the remainder of the cord by a double transection. In the second, homologous regions were excised and replanted to the same embryo. The spinal cords of the experimental larvae preserved for eight, twelve, sixteen, twenty and twenty-five days after the operation were compared with those of control larvae of similar age and length. No

evidence of localized cellular increases resulting from injury could be obtained at any stage. It is believed that the experimental data offer sufficient evidence for concluding that when cellular hyperplasias result from the interchange of various spinal segments between different levels the response can in no way be attributed to any stimulating effect of injury during the grafting.

WYMAN, Boston.

ACTIVE IMMUNIZATION IN NEUROSYPHILIS WITH AVIRULENT STRAINS OF SPIROCHETES. L. BENEDEK, Monatschr. f. Psychiat. u. Neurol. **79**:33 (May) 1931.

In this preliminary communication Benedek reports the results obtained in treatment for neurosyphilis with cultures of living spirochetes made by Hilgermann. The organisms were rendered avirulent by a method not yet available for publication. A suspension of these organisms was injected intragluteally in doses of from 0.5 to 1 cc. every two weeks. On improvement, the dose was reduced to 0.1 or 0.2 cc. to avoid a too rapid binding of antibody, which would leave the organism defenseless. Four patients with tabes, three with the tabetic form of dementia paralytica and five with dementia paralytica were treated. The patients with tabes and those with the tabetic form of dementia paralytica showed marked improvement; visceral crises and pains disappeared, and in two cases the mental condition was favorably influenced. Good results were not obtained in the cases of dementia paralytica. The author believes that inoculations with Hilgermann's avirulent cultures undoubtedly have a beneficial effect on the neurologic processes observed in neurosyphilis. Further investigations of this method of treatment are being carried out.

ROTHSCHILD, Foxborough, Mass.

SPINAL-GANGLION RESPONSES TO THE TRANSPLANTATION OF DIFFERENTIATED LIMBS IN AMBLYSTOMA LARVAE. R. L. CARPENTER, J. Exper. Zool. **61**:149 (Jan. 5) 1932.

The forelimb of Amblystoma punctatum may be transplanted successfully to a heterotopic position at periods of development ranging from early embryonic stages to metamorphosis. Such a limb will readily acquire connections with the circulatory and nervous systems of the host. The spinal ganglia of strange nerves innervating such transplanted limbs undergo hyperplasia similar in magnitude to that occurring when the limbs are transplanted before the outgrowth of peripheral nerves. The evidence indicates that the spinal ganglia respond to increases at the periphery throughout the larval period by the production of additional afferent neurons. Reduplications may occur in limbs transplanted heterotopically during the larval period, and vary from complete reduplication to the doubling of hands. Further evidence is derived to show that coordinated movements in heterotopic limbs occur only when there is at least partial connection with the normal brachial reflex correlation mechanism. The sequence of events leading to sensory hyperplasia and the source of the additional ganglion cells are discussed.

WYMAN, Boston.

UNILATERAL INTERMITTENT EXOPHTHALMOS. J. EUZIÈRE, E. DELORD, H. VIALLEFONT and J. VIDAL, Rev. d'oto-neuro-opht. **10**:689 (Nov.) 1932.

A patient with exophthalmos of the right eye was examined in April, 1932. The exophthalmos had begun eight months previously. At first the crises, lasting ten minutes, occurred once a week, but the frequency and duration had increased. The general, roentgenographic and laboratory examinations gave negative results, as did also examinations of the ears, nose and throat. Arterial tension was 15/9.5 (Vaquez). No facial or cephalic varices were observed. During the crises the globe was pushed forward and blocked in the median position; the crises were accompanied by diplopia, subjective noises, the latter of which were synchronous with the

cardiac pulsations, and vertigo. Compression of the jugular vein aggravated the exophthalmos, and compression of the carotid ameliorated it. Tonus in each eye was 15 mm. of mercury; retinal arterial tension was 150 mm. of mercury in the right eye and 50 mm. in the left eye. Treatment consisted of digital compression of the carotid artery. The patient was cured. The diagnosis lies between cavernocarotid aneurysm, orbital varices and vascular tumor.

DENNIS, Colorado Springs, Colo.

GLIOMA IN THE REGION OF THE LAMINA TERMINALIS WITH THE CLINICAL PICTURE OF A HYPOPHYSEAL TUMOR. OSKAR HIRSCH, Jahrb. f. Psychiat. u. Neurol. **48**:208, 1932.

A man, aged 30, had been suffering for two or three years from headache, dizziness and visual disturbances. Examination revealed a man of normal appearance with bitemporal hemianopia, genuine optic atrophy, an enlarged sella turcica and the chiasmatic cistern raised in a rooflike fashion over the diaphragma sellae (as evidenced by filling with iodized oil). There were no evidences of genital disturbances. At operation there was found a cystic cavity, which on being opened showed a portion of the brain prolapsed into it. Five days after the operation meningitis developed, and the patient died. Necropsy revealed a degenerated gliomatous cyst in the region of the lamina terminalis, a portion of which, the size of a bean, protruded into the third ventricle. The hypophysis was normal macroscopically as well as microscopically; the optic chiasm and both optic nerves were flattened and, together with the stalk of the hypophysis, were surrounded by the glioma.

KESCHNER, New York.

MAKING GOLD SOLUTION FOR SPINAL FLUID TESTS. B. S. LEVINE, Am. J. Syph. **16**: 103 (Jan.) 1932.

A gold solution of superior efficiency and reliable constancy may be made by following a recipe suggested by Levine. Five hundred cubic centimeters of distilled water is heated to 90 C., and 10 cc. of 1 per cent gold chloride solution is added. The mixture is reheated for one minute, and 6 cc. of 2 per cent potassium carbonate is poured in. This is shaken until the yellow color disappears and is set aside. A second flask containing 500 cc. of distilled water is heated, this time only to 60 C., and 5 cc. of fresh 1 per cent formaldehyde solution is added. After being shaken, this mixture should receive 2 or 3 drops of absolutely fresh hydrogen dioxide solution. This mixture is then poured rapidly into the first flask (containing the gold chloride and potassium carbonate). It is essential to shake the flask constantly while pouring. The mixture is first violet but soon becomes blue. When the color is ruby red, with a tinge of blue, and transparent by transmitted light, the solution is completed and ready for use.

DAVIDSON, Newark, N. J.

MULTIPLE TUBERCULOUS LESIONS IN THE BRAIN OF A CHILD (TUBERCULOUS ENCEPHALITIS). A. C. EDWARDS and A. W. WHITE, Am. J. Dis. Child. **43**: 396 (Feb.) 1932.

The authors claim that this presentation of the clinical and pathologic findings in the case of a Negro boy, aged 7, who died with generalized tuberculosis, warrants a diagnosis of diffuse tuberculous encephalitis. In the case reported there were found at autopsy five tuberculous lesions, from 0.75 cm. to 2 cm. in diameter, at various locations in the cerebral hemispheres, and also an early meningeal tuberculosis. The cerebral lesions, varying in size from that of a pinhead to that of a pea, were solitary and conglomerate tubercles, and the autopsy further revealed a meningo-encephalitis, general miliary tuberculosis and tuberculosis of the tracheobronchial lymph nodes. When the signs of menin-

geal involvement developed, death was only one month distant, but the entire course of the disease was six months.

None of the lesions apparently developed to a state of actual tuberculomas, and the case is of interest because of the rather diffuse involvement of the brain in a generalized miliary tuberculous process. LEAVITT, Philadelphia.

THE DIFFERENTIATION OF CHICK LIMB BUDS IN CHORIO-ALLANTOIC GRAFTS, WITH SPECIAL REFERENCE TO THE MUSCLES. ELEANOR A. HUNT, J. Exper. Zool. **62**:57 (May 5) 1932.

The limb rudiments of chick embryos were grown on the chorio-allantoic membrane of older chick hosts. The age of the donors varied from 2 to 7 days of incubation, and a series of grafts was obtained in which the total age ranged from 6 to 16 days. The muscles of the chick limbs are capable of initial independent differentiation, but they do not invariably maintain this independence. At a certain period, about the tenth day of incubation, some external factor seems necessary to continue the normal development and prevent fatty degeneration. Since the muscle in the grafts that were not innervated shows fatty degeneration, while in those that were innervated the muscle shows little or no degeneration, it is inferred that innervation is an important factor in the maintenance of normal muscle tissue. The skeleton of the chick limb is essentially self-differentiating, and at least after the third day the anlage appears to be a mosaic. Tendons and other fibrous formations occurred in the grafts to some extent, but frequently did not have a typical relation to muscle and bone. WYMAN, Boston.

ALZHEIMER FIBRILLARY CHANGES IN THE BRAIN STEM OF A PATIENT AGED 28 WITH A POSTENCEPHALITIC CONDITION. I. FENYES, Arch. f. Psychiat. **96**:700 (May) 1932.

The author presents the case of a woman, aged 28, with a history typical of encephalitis, a parkinsonian posture, propulsion and retropulsion and other signs of a parkinsonian syndrome, as well as psychotic phenomena. Autopsy showed fatty degeneration of the ganglion cells in the cerebral cortex and brain stem, sclerosis, disappearance of cells, etc. with moderate lymphocytic infiltration in the vessels of the brain stem. There was a diffuse fibrillary change of the Alzheimer type in the brain stem and a pronounced affection of the substantia nigra. In the psychotic picture there were no symptoms typical of the Alzheimer presenile mental disturbance, and no senile plaques were found. The author groups this case along with those noted by Schaffer (28 years) and by Malamud and Lowenberg (23 years), as representing the earliest age at which Alzheimer fibrillary changes have been found, and points out that it is the only case in which a parkinsonian syndrome has been associated with this type of histologic change. MALAMUD, Iowa City.

CHEMICAL STIMULATION BY SALTS IN THE OYSTER, OSTREA VIRGINICA. A. E. HOPKINS, J. Exper. Zool. **61**:13 (Jan. 5) 1932.

A method of studying accurately the latent period of the reactions of the oyster to chemical stimulation is described. Tests of the latent period of reaction of the tentacles of the oyster were made with twenty-one salts, comprising most of the chlorides, iodides, bromides, nitrates and sulphates of potassium, sodium, ammonium, lithium and magnesium. In general, the effectiveness of an ion in stimulation depends in a direct manner on atomic weight. The cations fall into the same order according to atomic weight and to stimulating efficiency, except that the ammonium and sodium are in reverse positions in the two series. The anions fall into the same order according to atomic weight and to efficiency in stimulation. If the results are plotted graphically with the reciprocal of latent-period values as ordinates, and atomic weight multiplied by mobility of ions as

abscissas, both the series of anions and the series of cations fall into the same regular ascending order. Sensory stimulation of the tentacles of the oyster by the salts employed is primarily a function of the cations. WYMAN, Boston.

THE CERVICAL SYNDROME IN CLOSED TRAUMATISMS OF THE SKULL. L. CRUSEM, Rev. d'oto-neuro-opht. **10**:656 (Nov.) 1932.

The principal complaints common to the posterior cervical syndrome and the syndrome of traumatism of the skull are headache, vertigo, tinnitus, nervousness and visual disturbances. Ten patients with long-standing traumatisms of the skull were studied with reference to the cervical syndrome. A certain number remembered a severe pain or stiffness in the neck following the accident, and, in most of them, the stiffness and tenderness of the neck and over Arnold's point were found on one or both sides. Roentgenography revealed osseous cervical lesions in some cases; in others an arthritis could not be differentiated, and in one the vertebrae were normal. Direct trauma in the cervical region could be excluded in all. The cervical column bears the brunt of all blows on the skull and is often the first to suffer the consequences of such trauma. It should be subjected to painstaking examination in all cases of cranial traumatism. In a certain proportion of the cases of cranial traumatism the subjective syndrome is in reality a cervical syndrome. DENNIS, Colorado Springs, Colo.

THE DEVELOPMENT OF THE BRAIN OF AMBLYSTOMA (3 TO 17 MM. BODY LENGTH). R. C. BAKER and G. O. GRAVES, J. Comp. Neurol. **54**:501 (April) 1932.

This paper deals with the external and internal configurations of the brain of Amblystoma larvae, the disposition of nuclear and fibrillar material and the early appearance of the latter in brains selected at critical stages. Wax models were made by the Born and Peter method based on complete serial sections. The earliest stage presented is shortly after the closure of the neural tube, with its partly included neural-crest cells and the optic vesicles widely evaginated from the brain proper. In the series of selected stages that follow, the general change of brain contour, the development of the forebrain, the appearance of evaginations (cerebral hemispheres, epiphysis, paraphysis and mamillary bodies), the increase in ventricular surface and its molding and the chronological appearance of fibrillar material in the brain regions are described. The oldest larva figured shows well developed cerebral lobes. All parts of the adult brain except the infundibulum have made their appearance by the time the animal has reached the body length of 17 mm. ADDISON, Philadelphia.

METHOD FOR THE RAPID DEMONSTRATION OF SENILE PLAQUES. P. DIVRY, Riv. di pat. nerv. **40**: 489 (Sept.-Oct.) 1932.

Divry describes a method which, with no pretension of being superior to others, already known, has the advantage of a rapid execution. The material is fixed in formaldehyde, the duration of fixation being unimportant. Frozen sections, of 20 microns, are received in water, and then transferred to a porcelain capsule containing a silver solution composed of: Hortega's fluid (ammoniacal silver carbonate as currently used for impregnation of microglia), 5 Gm.; distilled water, 5 Gm.; pyridine, 10 drops. The capsule is heated, with gentle agitation of the section, until the first vapors arise, when the section becomes more or less brown. The section is transferred with a glass rod into a 10 per cent solution of neutral formaldehyde. Reduction is very rapid, almost instantaneous. At times, reduction is more definite if the section is transferred into distilled water before the reduction into formaldehyde. As the method does not involve the formation of precipitates, the therapy with gold may be omitted and the section mounted in gelatin-glycerin. FERRARO, New York.

THE THEORY AND THERAPY OF THE SYMPTOMS OF WITHDRAWAL IN CHRONIC MORPHINISM. ALEXANDRA ADLER, Jahrb. f. Psychiat. u. Neurol. **48**:105, 1932.

According to the author, the symptoms of withdrawal in chronic morphinism are due to water retention. To regulate this disturbance in water metabolism, an attempt was made to employ a drug with definite central as well as peripheral action. Theophyllin-ethylenediamine was found to fulfil these indications. Its effects were compared with those of urea, mersalyl and merbaphen, and it was found that all of these drugs have only a peripheral effect. Fifty cases of chronic morphinism "cured" (the quotes are inserted by the abstractor) by the administration of theophyllin-ethylenediamine are reported. The treatment consisted of two daily intravenous injections of 0.24 Gm. during a period varying from two to eight days. Following this treatment there was marked improvement in the subjective and objective symptoms of morphine withdrawal. These patients had previously been treated by other "withdrawal cures" with little or no effect.

KESCHNER, New York.

THE SPINAL FLUID AFTER MALARIA THERAPY. WALDEMIRO PIRES and CERQUEIRA LUZ, Encéphale **27**:703 (Sept.-Oct.) 1932.

Examination of the spinal fluid made after malarial treatment does not furnish definitive information for judging the efficacy of treatment. The abatement in serologic signs may be observed only after several months; a patient clinically cured may present positive reactions. After a year, however, there is a certain parallelism between the clinical remissions and the serology. Dujardin, who is quoted, maintained that complete integrity of the spinal fluid is not only slow in being achieved but is relatively uncommon; moreover, that numerous cases of dementia paralytica considered cured present again spinal fluid findings. An irreducible spinal fluid is, nevertheless, a bad prognostic sign; reinoculation is indicated. A favorable action on the fluid with unchanged clinical course usually is a bad index and points to a return of positive serology. Those recipients who achieve simultaneous clinical remission and negative fluids ordinarily do have a relapse.

ANDERSON, Los Angeles.

LIPODYSTROPHY: ATROPHY AND TUMEFACTION OF SUBCUTANEOUS TISSUE DUE TO INSULIN INJECTIONS. A. H. ROWE and O. H. GARRISON, J. A. M. A. **99**:16 (July 2) 1932.

Rowe and Garrison review the literature on lipodystrophy following injections of insulin and report that during the last nine years they have observed two instances of this condition. Recently they have carefully examined the tissues of fifty patients whose ages varied from 7 to 79, with an average age of 40.6 years, and who had taken insulin for an average of one year. Definite atrophy was observed in two additional cases. The absence of atrophic reaction in more of the patients may be due to the emphasis the authors have always laid on the importance of variation in the site of injection. Definite fatty atrophy of subcutaneous tissue occurred in one patient who had received pollen therapy in the same area once a week for ten months. This corroborates the opinion of Lawrence that mechanical injury of the fatty cells may be the true cause of the atrophy.

EDITOR'S ABSTRACT.

A CASE OF MENINGIOMA OF THE OLFACTORY GROOVE. SYNDROME OF THE ANTERIOR COMMISSURE (?). E. GAMPER, Nervenarzt **5**:518 (Oct. 15) 1932.

Gamper reports a case of meningioma arising from the olfactory groove, which differs from the cases usually seen in that the patient was rather young (aged 27) and primary optic atrophy was lacking. The outstanding early symptoms consisted in a gradual loss of interest and in akinesia. During bouts of severe headache the patient was subject to peculiar movements of the head and lips similar to

those observed in animals, particularly the rabbit, during the act of eating. Smacking movements characteristic of an uncinate fit were not observed. Surgical exploration was terminated when cerebral softening was discovered; this seemed at the time to confirm the preoperative diagnosis of a glioma of the frontal lobe, although it was later found to be the result of compression of the anterior cerebral arteries. The author expresses the view that the peculiar seizures might be accounted for by stretching of the anterior commissure by the upward growth of the tumor.

DANIELS, Denver.

PHOBIAS: I. A. R. REDFERN, Brit. J. M. Psychol. **11**:295, 1932.

Individual psychology groups phobias, compulsions and hysterias together as phenomena liable to occur when the desire for personal superiority is threatened; the ego ideal is preserved by recourse to neurotic manifestations. The rôle of the therapist, as described in the case history given, is a passive one, an attitude of objective friendliness. The use of this technic in treatment is stated as being based on the adlerian principle that the discovery by the patient of his own hidden life plan is the most important part of therapy. The patient is told that cure will come about, if at all, as a result of his own capacity for cooperation and free discussion of his problems.

PHOBIAS: II. SYBILLE YATES, Brit. J. M. Psychol. **11**:301, 1932.

Phobia is defined according to the freudian concept as a specific form of hysteria in which regression occurs following deprivation at the phallic stage of libidinal development. There is a strongly ambivalent attitude toward the desired love object with accompanying feelings of guilt. The phobia is seen as a symbolic substitute for the desired object. A change of affect is brought about, so that the anxiety now finds expression in conscious fear of the object of the phobia, and by projection the ego is enabled to evade the intrapsychic conflict. A comprehensive, although brief, case history is given, in which the development of a mouse phobia from the original problem of emotional deprivation in childhood is described. The factors determining the specific features of the phobia are traced via the infantile psychologic pattern and the external contributing circumstances of the life history. It is described how, in the structure of the phobia, expression is given to the repressed affects and how the phobia serves, to some extent, to placate the demands of the super-ego and to lessen feelings of guilt.

PHOBIAS: III. JAMES CARRUTHERS YOUNG, Brit. J. M. Psychol. **11**:309, 1932.

Young postulates that a phobia is determined by the immediate situation in a person presenting diathetic disorders, probably of the nature of organic inferiority or dyplastic development, with a resultant impoverishment of mental and physical life.

ALLEN, Philadelphia.

PHOBIAS: IV. EMANUEL MILLER, Brit. J. M. Psychol. **11**:314, 1932.

This article presents a discussion of the preceding three papers. In all cases in which guilt motives are productive of neurosis, the ego idea is the center of reference for all behavior. When the diffused anxiety is not canalized off, as in phobia formation, complete withdrawal from reality can follow. The writer raises the question here as to whether the latter may be the way the introvert handles the intrapsychic conflict, indicating that a fundamental difference of type determines what reaction may occur.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, April 20, 1933

PERCIVAL BAILEY, M.D., *President, Presiding*

PARENCHYMATOUS CORTICAL CEREBELLAR ATROPHY (CHRONIC ATROPHY OF PURKINJE'S CELLS). DR. HARRY L. PARKER and DR. JAMES W. KERNOHAN, Rochester, Minn. (by invitation).

Cerebellar atrophy commencing after middle age is relatively rare; only a few examples have been described, mostly in foreign literature. The type coming under the title of this article has been described by various authors during the last thirty years. Eleven cases have been studied and reported, so that with the addition of our own case there are twelve instances in which complete clinical and pathologic studies have been made.

The disease is not familial, nor is it confined to either sex. Symptoms begin to appear at some time between 40 and 60 years of age; following a slow, insidious onset there is a steady progression over a period of years to complete helplessness and death from some intercurrent disease. The clinical picture is essentially that of slowly increasing ataxia, which appears first in the lower extremities. In about half the cases the trunk, upper extremities and speech organs become progressively involved. Tremor and nystagmus are usually absent. Mentally, the patients are well preserved, and symptoms of senile degeneracy or of arteriosclerosis of the central nervous system are lacking.

At necropsy the cerebellum, in the majority of instances, appears to be atrophied and has been described as being reduced by one-third or one-fourth its normal size. In some cases, however, it is normal on gross inspection. The microscopic changes are confined in the main to the Purkinje cells, with their disappearance over a large area of the cerebellar cortex. In the remaining areas they are shrunken and have undergone all stages of disintegration. In many cases the destruction of the cells has been relatively more marked on the superior surface of the cerebellum, and more so in the anterior portion of the vermis cerebelli and in the quadrilateral lobule. The basket cells are well preserved, and only little change is to be observed in the molecular and granular layers; the central white matter and dentate nucleus are completely normal. In some cases a gliosis can be seen in the white matter of the folia of the cerebellum, ending abruptly as it joins the central white matter. In our case some slight gliosis was found around the dentate nuclei and in the granular layers, and a more marked gliosis was present in the nerve fiber layers. The inferior olivary nuclei and their cerebellar connections are in most instances intact. Altogether, the most striking change is the almost complete annihilation of the Purkinje cells, with remarkably little else to comment on.

The essential cause of the disease remains unknown. Premature senile disintegration of the Purkinje cells, antecedent toxic or infectious processes, chronic alcoholism and a specific virus disease have each been considered as possible causes, without enough evidence to incriminate any of them.

DISCUSSION

DR. THEODORE T. STONE: For the past two years I have been studying in detail two cases that present the same clinical syndrome although they do not

belong to the group Dr. Parker described, having, in addition, a definite familial history. In the first case a brother and an uncle of the patient were similarly affected. In the second case, the father of the patient presented the same condition. The disorder did not appear in my patients in the later decades, as in Dr. Parker's patients, but produced pure cerebellar signs and symptoms in the latter part of the third decade, at the ages of 38 and 39 years, respectively. Both patients are male. Both are alive. One has had the condition for five and a half years and the other for four years.

In addition to all the signs and symptoms pointing to cerebellar involvement I found nodding of the head, nystagmus, loss of abdominal reflexes and increased deep reflexes. The pons and olivary bodies were not involved. One patient had ataxia when first seen, which I could not connect with any syndrome with which I was familiar. I found that, in 1907, Gordon Holmes had described a familial form of cerebellar degeneration. Many authors have reported the pathologic changes described by the essayist; the most important change was the atrophy or absence of all Purkinje cells.

DR. J. T. NERANCY, Elgin, Ill.: In view of the fact that Dr. Parker mentioned that various pathologic processes may play a rôle, does he attach any significance to the fact that the patient had influenza at the age of 56, when the disturbance seems to have become noticeable?

DR. HARRY L. PARKER: As I mentioned, the disease in question is not familial. Nevertheless, I am glad that Dr. Stone reviewed the cases which he has observed; they resemble closely those in the series described by Gordon Holmes in 1907. In these cases the condition has a familial character and is in nice contrast to the condition I am describing, which appears in only one member of the family.

The outstanding feature of the disease is the selective massive destruction of the Purkinje cells. During my study of the reports of other cases, as well as of our own case, it occurred to me that possibly the Purkinje cell system has a higher relative degree of vulnerability. Reviewing other degenerative diseases in the cerebellum, including those described by Gordon Holmes, there is no doubt that, whatever else is damaged, the Purkinje cells undergo more than their share of change. Work has been done also that tends to show that the Purkinje cells normally begin to disintegrate rather early in life; from the fifth decade on there is an increasing reduction in their number, completely out of proportion to that of other cells in the cerebellum.

I have been asked as to the influence, if any, of the antecedent influenzal attack in the case of our patient. An infectious origin has been invoked by numerous writers; yet nothing of an inflammatory nature can be seen in the microscopic preparations. In some of the northern counties of England, sheep suffer from an acute epidemic infectious process locally called "louping ill." This peculiar disease attacks specifically the Purkinje cells of the cerebellum. It is considered to be due to a specific virus, which has been transmitted experimentally to mice, dogs and monkeys. Nothing quite analogous, however, has yet been reported as occurring in a human being. It is possible that a variety of causes may be to blame; they may differ in one case as compared with another.

NINETEEN CASES OF INTRACRANIAL LESIONS. DR. ALBERT W. BRYAN, Madison, Wis. (by invitation).

The recognition, localization, identification and eradication of degenerative or invasive intracranial processes present many difficulties to those who do not see such numbers of cases as appear in the large medical centers but who, nevertheless, must frequently deal with these conditions. In illustration I present reports of a small group of cases in rather typical locations. Preliminary impressions and diagnoses from various sources, erroneous in some cases, are given. The information available from encephalography and ventriculography is given in a number

of instances. The material is derived from cases studied by courtesy of the staff of the Wisconsin General Hospital, as well as from those in my own service at the Jackson Clinic; in some cases further information has been supplied by the staff of the Mayo Clinic.

The group of cases has been chosen mainly because of the opportunity to check the terminal pathologic picture against the presenting clinical picture. In three cases the lesions involved the frontal area; in five, the temporoparietal region; in one, the third ventricle; in five, the cerebellopontile angle, although only one of these was a neurofibroma, the others in the group tending to invade the nearby structures, especially the third and fourth ventricles; in two, there were cerebellar tumors; in two, cerebellar abscesses; in one, an intramedullary lesion of the upper part of the spinal cord.

The important symptoms, signs and serologic studies and the preliminary diagnosis as compared with observations at operation and at autopsy are shown in the accompanying lantern slides. Certain cases may be outlined in more detail. In case 2, a clinical picture suggesting multiple lesions was confirmed at autopsy by the finding of multiple neurofibromas invading the skull, cortex and cerebellopontile angle. An encephalogram had shown an increase in the supracallosal air, air in the sulcus and dilatation of the chiasmic cistern, but no ventricular shadow. A ventriculogram showed marked internal hydrocephalus, thus confirming the diagnosis of a lesion of the posterior fossa and illustrating the value of roentgenologic studies.

Somewhat similar roentgenologic findings were noted in case 13, in which an adenoma from the choroid plexus involved mainly the cerebellopontile angle.

Case 7 was of interest because of a rather inconspicuous history of attacks of petit mal, with hypertension and blood urea of 90 mg., suggesting cardiorenal disease with associated cerebral confusion and a consequent fall. This was followed by choked disk on the right and weakness of the left arm and leg. At operation a straw-colored fluid, as from a degenerating neoplastic process, was found. At autopsy, some months later, a large infiltrating neoplastic mass, histologically a spongioblastoma multiforme, was found in the right temporal lobe. This condition, in which the findings strongly suggested a cardiorenal illness, but were later determined to be those of a tumor of the brain, is in contrast to that in which malignant hypertension may masquerade as a tumor of the brain.

Case 9 presented marked bilateral choked disk, with an associated spinal fluid pressure of 70 cm. of water, transient intellectual symptoms varying with the control of the intracranial pressure and variable asynergia. This case suggests the probable value of a frank use of ventriculograms. This is emphasized by the negative results from a cerebellar decompression and the fact that only 15 cc. of ventricular fluid was removed from the left ventricle at the time of operation whereas at autopsy, seven weeks later, a supratentorial tumor was found closely applied to the medial surface of the parietal lobe and associated with a degenerating cyst, the size of an orange, filled with yellow fluid, which occupied the normal site of the right ventricle. Ventriculography might well have revealed the degenerating cyst and have prevented a useless cerebellar exploration. Histologically, the growth was a spongioblastoma multiforme.

In case 19, there was some retention of iodized poppy seed oil in the cisterna magna, associated with a clinical picture of an upper motor neuron lesion involving the left leg and a lesion of a lower motor neuron affecting the left arm, with bilateral sensory disturbances. That the lesion was extramedullary was suggested by the fact that symmetrical neurofibromas were distributed over the forearms and thighs. Following an extensive cervical laminectomy there was clinical improvement, but eight weeks later there was rapid medullary failure. At autopsy, an infiltrating lesion, occupying all but a narrow periphery of normal cord tissue and extending the length of four cervical segments, was found. Histologically, this tumor was a spongioblastoma multiforme, a lesion which is rare in the spinal cord, although perhaps the commonest of cerebral gliomas.

The duration of the clinical course of the gliomas in this small group may be compared with that of the large group reported by Cushing. It is of interest that in five spongioblastomas the average total duration was sixteen months, as compared with twelve months for the hundred cases reported by Cushing; two medulloblastomas in this series averaged fourteen months, whereas forty-one cases in Cushing's series averaged seventeen months; three patients with astrocytomas lived in excess of fifty-one months, whereas forty-one of Cushing's patients lived in excess of eighty-six months. This observation emphasizes in a small way the value of histologic diagnosis in relation to prognosis.

The danger of disturbing the spinal fluid balance by cisternal puncture or ventriculography when there is reason to suppose that a lesion exists in the posterior fossa was illustrated in the series; yet the desirability of ventriculograms in such cases is so great that it is important to perfect the diagnostic management in these cases so that freer use will be made of these methods both preoperatively and postoperatively. Maintenance of the head in the dependent position for forty-eight hours after the procedure may be of value. It is indicated that ventriculography should not be undertaken unless the reports can be made available immediately and necessary surgical procedure undertaken forthwith.

DISCUSSION

DR. PERCIVAL BAILEY: I was interested to hear that a tumor in the upper region of the spinal cord caused the patient to complain of pain. Pain is not generally considered to be a striking feature in cases of intramedullary tumor; yet I have recently read the records of some hundred cases in the literature and find that 60 per cent of the patients complained of pain, often of a radicular nature, girdle sensations around the body or pain in the extremities. One cannot depend more on that symptom to make a differentiation between intramedullary and extramedullary tumors than on other symptoms.

It is remarkable that a lesion of the size of the spongioblastoma in the occipitoparietal region could lie there without producing some defect in the visual field. The visual fields may not have been carefully examined. Such a lesion in the posterior fossa is very rare, and the visual findings should make the differentiation.

DR. HARRY L. PARKER, Rochester, Minn.: Dr. Bryan mentioned that there were mental changes in a patient who had a tumor of the cerebellopontile angle, and that this change led to the mistaken idea that the process was supratentorial. Tumors below the tentorium are ordinarily not considered a common source of mental deterioration. However, I recall cases in which rather marked mental changes led us astray in diagnosis. In a patient with an acoustic neurofibroma, without signs of increased intracranial pressure, the mental changes were so definite that they led to legal difficulty after the death of the patient regarding the validity of her will and the disposal of her property. Dr. Bryan is to be congratulated on the careful study of his cases and his earnest attempt to classify the results.

DR. ALBERT W. BRYAN: I hope to study the data more fully and may report some of the cases in full at a later date.

TATTOOING AND ITS RELATION TO INVERSION AND PERVERSION. DR. FRANCIS J. GERTY.

This article will be published elsewhere.

PSYCHOANALYSIS OF A MANIC-DEPRESSIVE PATIENT (WITH CASE PRESENTATION). DR. CLARENCE A. NEYMANN.

This article will be published elsewhere.

Annual Meeting, May 18, 1933

PERCIVAL BAILEY, M.D., *President, in the Chair*

MULTIPLE SCLEROSIS (PRESENTATION OF A CASE). DR. GEORGE W. HALL.

My colleagues and I have encountered some difficulty in classifying cases of multiple sclerosis. Many present a rather advanced state of the disease, while the early symptoms demand consideration of acute encephalomyelitis; others present a syndrome similar to subacute combined degeneration of the cord, and syphilis of the central nervous system must also be excluded. The laboratory findings are of assistance in arriving at the proper diagnosis. The excuse for presenting this subject is to call attention to the so-called quinine treatment first advocated by Brickner (ARCHIVES OF NEUROLOGY AND PSYCHIATRY **28**:125 [July] 1932).

In estimating the value of this method of treatment, I wish to emphasize the difficulties arising from the common natural remissions and exacerbations. I believe, however, that this treatment is of value in the case I am presenting here.

For five months the patient had been unable to control the bladder or bowels; he had gradually reached the stage at which he could scarcely move a finger or a toe. He has received quinine hydrochloride since July, 1932, and he is now able to walk on crutches, has good strength in his limbs and shows no difficulty in controlling the bladder and bowels. I have similar records of advanced cases, in some of which the patients have been able to resume regular work. The important observation has been that patients who have responded to this treatment, combined with a series of intravenous injections of sodium cacodylate, have showed a gradual and continuous improvement and have not had exacerbations such as one usually observes in most cases.

DISCUSSION

DR. ARTHUR WEIL: Brickner states that following this treatment the symptoms that appeared last disappeared first. What is your opinion?

DR. GEORGE W. HALL: Brickner does make that statement, and I think that it is true in most cases. I expected to present another patient this evening, however, who showed a bilateral Babinski sign rather early. She was a telephone operator and had to stop work for several weeks because of clumsiness in using her hands and disturbance of gait. She has returned to work, and there is only a suspicion of a Babinski sign, although that was an important early sign and was present when I first examined her.

DR. JAMES G. GILL: How long had the symptoms been present before treatment was instituted in this patient?

DR. GEORGE W. HALL: In forty or fifty records there is a great variance in this respect. In some cases the symptoms start suddenly and make one think of acute encephalitis or encephalomyelitis. In this man the symptoms developed gradually; they were present for several months before the treatment was begun.

DR. ROY GRINKER: There is no disease in which it is so hard to evaluate treatment as in multiple sclerosis. The varying nature of the diseases classified under multiple sclerosis raises another important difficulty in the discussion of effects of treatment. As Dr. Hall intimated, one does not know whether the case is one of acute disseminated encephalomyelitis. Dr. Bassoe and I tried to show from the classification of the various syndromes which might be made of the various so-called inflammatory diseases of the central nervous diseases that one has to include in each pathologic class various clinical types of diseases. Some might be called chronic multiple sclerosis; others, acute multiple scelrosis, and others, dis-

seminated encephalomyelitis. From the standpoint of clinical diagnosis it is difficult to determine whether this or any other patient might have a first attack of disseminated lesions, falling under the classification of disseminated myelitis, and never have another attack without any treatment.

What does Dr. Hall now think of the fever therapy for multiple sclerosis about which he was so enthusiastic some years ago?

DR. GEORGE W. HALL: The fever treatment is of value, and I still use it in many cases. I do not use it so much at present, as it behooves one to try other methods and adopt them if they prove to be more efficient.

PATH OF PUPILLARY LIGHT REFLEX. DR. S. W. RANSON.

This paper will be published in full in a later issue of the ARCHIVES.

USE OF IODIZED POPPY SEED OIL FORTY PER CENT IN DIFFERENTIATION OF LESIONS OF THE CONUS AND CAUDA. DR. HENRY HARKINS (by invitation).

This article will be published in a later issue of the ARCHIVES.

DISCUSSION

DR. GEORGE W. HALL: I observed a case which proved to be one of tumor of the cauda equina. A lumbar puncture above the tumor revealed evidence of a block. Examination of the fluid showed a heavy globulin content with few cells, which no doubt kept the fluid from receding in the tube when the pressure on the jugular veins ceased.

RESULTS OBTAINED BY DESTRUCTION OF THE RED NUCLEUS. W. R. INGRAM (by invitation).

This article will be published elsewhere.

AN UNUSUAL TUMOR OF THE THIRD VENTRICLE. DR. W. B. HAMBY (by invitation).

This article will be published in a later issue of the ARCHIVES.

CURRENT CONCEPTIONS OF STUTTERING: A CRITICAL ESTIMATE. DR. MEYER SOLOMON.

From a review of the various theories (anatomic, physiologic and psychologic) of stuttering I reach the following conclusions: Stuttering is a disorder related to the emotions and the personality. It is due to emotional disequilibrium in social situations requiring speech, with a consequent struggle to maintain or regain equilibrium and an accidental stumbling into stuttering, which becomes a conditioned emotional response in social situations involving the use of speech.

Emotional disequilibrium during speech in social relations may be induced by many factors of a psychologic nature responsible for undue stress, tension and strain. Fear of recurrence of difficulties of speech and transformation of the personality ensue. Intensive study and treatment of personality are indicated. Stuttering should be studied and managed in its earliest phase. Stuttering in preschool or school children requires careful study of the child's habits, the technic of child management, the home, the neighborhood and the school influences, with special search for causes of undue pressure and tension.

DISCUSSION

DR. A. B. YUDELSON: Has Dr. Solomon noticed that stutterers are inclined to be talkative, to a certain extent tending toward garrulousness? From the premise, as noted by many, is it not true that stutterers are impulsive personalities who

try to say two or more words at a time to make sure that they are going to express their ideas so as to make them attractive to the listener, and also to make them clear? They are rather particular as to how they will transmit the idea to make it clear. In as many cases as I could be induced to observe and treat I have found that if these patients are taught to speak one word at a time, not to indulge in extensive explanations which overexplain, and to exercise sufficient control over themselves to do away with their impulsiveness, they do away with the verboseness as well as with the stuttering.

DR. ALFRED P. SOLOMON: Dr. Meyer Solomon's criticism of the freudian approach seems to represent a resistance to the literal interpretation of freudian terminology. Some of us with freudian leanings find it much more convenient to regard the terminology as purely descriptive, yet having definite comprehensive and tangible meanings. During Dr. Solomon's presentation of his emotional theory, with which for the most part I am heartily in accord, I found that it was easy to translate it into freudian terms. When this was done I found that his interpretation of stuttering is comparable to that of the psychoanalytic approach in any of the psychoneuroses.

DR. MEYER SOLOMON: There is much in what Dr. Yudelson said. However, this condition occurs in children of other types. For two years I have studied one child who is calm and easy-going, and yet has become a stutterer. This symptom is more apt to occur in the timid child; the aggressive, "hard-boiled" child is not so likely to stutter. If a timid child is embarrassed for some reason, tries to use a vocabulary beyond his powers, is teased by other members of the family, does not get a chance to talk in the family discussions and the like, stuttering is likely to occur. It may occur in the impulsive type of child also. The impulsive child will try to tell a whole sentence in the same breath; there is a tendency to say too much in a short time, and when he is not naturally impulsive in speech the stutterer may become so because he is afraid that he will have trouble in speech. I do, however, believe that the average person having this disorder needs to be encouraged to be calm, to say less and not to begin talking unless he has something definite in mind, since often a stutterer will begin to talk before he has formulated his ideas and will try to say too much.

Why should one be forced to use freudian terms? If the terms are etiologic, that is different; further than that, the use of freudian terms is not necessary. After all, the usual goal of a freudian analysis is to prove that sexuality or eroticism is at the basis of disorders of behavior. If freudians used ordinary terminology, there would not be any disagreement about it. Most workers on speech do not accept the freudian views.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, May 26, 1933

A. C. BUCKLEY, M.D., *President, in the Chair*

A CASE OF THROMBOSIS OF THE VERTEBRAL, BASILAR AND INTERNAL CAROTID ARTERIES. DR. T. SHALLOW and DR. M. A. BURNS.

History.—E. H., a white housewife, aged 24, was admitted to the Jefferson Hospital on Dec. 5, 1932, because of intermittent attacks of paralysis of nine weeks' duration and crying spells which had occurred for more than two years. The father had died of diphtheritic paralysis; the mother was living and well; one nephew had diabetes, and all the relatives were of a nervous temperament. There was no history of cancer, tuberculosis or cardiorenal disease. The patient had had the usual diseases of childhood, and at the age of 5 years had diphtheria. For three years before admission to the hospital she had edema of the feet and ankles, and

for six years before she was seen by us she had numbness and a pricking sensation in the left leg and foot. This gradually became worse until two years prior to examination, at which time it involved the entire left extremity to such an extent that the patient could stick it with a pin without feeling pain. There was a tonsillectomy at the age of 22, but no other serious operations or injuries.

The present illness began eleven weeks before admission, with paralysis of both legs and arms and numbness in the back of the neck. It was possible, however, for the patient to move the arms and legs with difficulty. In two weeks she was able to be up and could walk across a room, but after that she grew progressively worse and became more paralyzed. Three weeks before the onset she had slight vomiting with nausea, and one week later there was another period of vomiting with nausea lasting for three or four days. She was in bed; the legs and arms were numb and paralyzed, but gradually they improved, and she was able to sit up in a chair, although she could not do any work and could not feed herself. On Dec. 1, 1932, she experienced difficulty with speech. She lost control of the left side and could move it but slightly. When taken to the hospital on December 2 she could not walk or talk.

Examination.—The patient was helpless, able to move only the left arm, head and eyes. She could not talk. The heart and lungs were normal.

Neurologic examination revealed a left facial palsy. There seemed to be a nystagmoid movement on looking to the right and left. There was complete motor aphasia. The olfactory sense and the sense of hearing were apparently unimpaired. There was complete motor palsy on the right side in the upper extremities, and weakness on the left. The deep reflexes were decreased; there was no sensory disturbance. The abdominal reflexes were lost. In the lower extremities there were complete motor palsy on the right and definite weakness on the left. The patellar reflexes were more prompt on the left. On the right side there were a fleeting ankle clonus, a definite Babinski sign and a Chaddock sign. Sensation was undisturbed.

Examination of the eyes revealed equal pupils which reacted normally to light, in accommodation and consensually. Associated movements were unimpaired to the right, above and below. There was loss of associated movements to the left, with a coarse nystagmus on looking to the right. Except for haziness and paleness of the fundi, the fields appeared normal. Roentgen examination of the skull revealed nothing abnormal. Laryngoscopic examination was unsatisfactory because of the inability of the patient to cooperate; a thick secretion was present in the pharynx, and there was lack of sensibility of the pharynx and the laryngopharynx. Roentgen examination of the spine gave negative results, and special studies of the blood showed nothing abnormal.

Clinical Diagnosis.—From the clinical findings the lesion was thought to be in the left side of the pons.

Course.—On December 6 the patient's temperature began to rise and continued to do so until December 8, when pulmonary edema developed and the patient died.

Postmortem Examination.—The cerebral dura was normal. The superficial vessels of the pia-arachnoid were injected over the vertex, but no evidence of thrombosis of these vessels was observed. The meninges were not inflamed. When the brain was removed, the vessels at the base of the skull were found to be somewhat thickened, and the two vertebral and the basilar arteries were thrombosed. Both internal carotids seemed somewhat thickened, and the vessel on the left side was thrombosed. The brain weighed 1,070 Gm., and measured 17 by 14 by 8 cm. The brain was of normal consistency and contour, and on section through the frontal, parietal and occipital lobes no evidence of a lesion was observed on either side. The ventricles appeared normal and were not distended. On section of the brain, no lesion was observed, such as softening or hemorrhage. A portion of the fourth ventricle was dilated. Small cerebral vessels just beneath the floor of the left lateral ventricle were thrombosed.

DISCUSSION

DR. T. A. SHALLOW: Information additional to that furnished by Dr. Burns in the history of this case is the result of a postmortem examination. The entire vascular tree, except the blood vessels at the base of the brain—the vertebral and those of the circle of Willis—was entirely normal. We were able by hydrostatic pressure introduced into the aorta, with both common carotid arteries compressed, to force the clot from the right vertebral artery.

The assumed presence of local vascular disease dating from the age of 18 is significant. Vascular pathologic changes in advanced age, associated with generalized arteriosclerosis, are common, but from the history of this patient, there was a symptom group which resembled hysteria beginning at the age of 18 years and finally producing death. There is a certain basis for interpreting some of the symptoms as due to local angiospastic anemia.

For six years the patient had numbness and a pricking sensation in the left leg and foot, which gradually grew worse until, at the end of four years, it involved the entire left lower extremity. The patient could stick a pin in her leg and have absolutely no sensation. A diagnosis of hysteria was made. The question arises: Did she have hysteria, or did she have involvement of the spinothalamic tract at its termination in the base of the brain? In favor of the last conclusion are the photomicrographic reproductions of the blood vessels at the base of the brain. which show that she had extensive thrombo-angio-arteritis. It could be argued that this was preceded by local angiospastic disorders, similar to that observed in the extremities in Raynaud's disease. The illness three months before death began with weakness of both legs and arms. She was able to move the arms with difficulty. When one seeks the site of a lesion which could produce this symptom complex, a purely motor one and not associated with any sensory disturbance previously described, because the numbness and lack of sensation had entirely disappeared for two years, one would select the area in the medulla and the decussation of the pyramids. That this disorder began as a local vascular spasm is indicated by the fact that two weeks after the onset she was able to walk across the room without assistance. Another significant suggestion that angiospasm played a part in producing these symptoms in the beginning was the fact that in addition to the motor palsies she again began to have numbness of both legs and arms, owing to a lack of blood supply to the spinothalamic area in the base. Both of these motor and sensory disturbances gradually improved so that the patient was again able to be up and about her home.

On Dec. 1, 1932, two months after the beginning of the last attack, it was noticed that there was difficulty in speech, which gradually developed into aphonia; with this there was entire loss of motor power on the left side. We concluded that the nucleus of articulation, the twelfth or hypoglossal and the ninth or glossopharyngeal nuclei, were involved because of lack of blood supply. It was noticed on admission to the hospital that the head drooped to the left. This was interpreted to mean paralysis of the spinal accessory nucleus. We therefore feel confident in making the diagnosis of thrombosis of the vertebral artery with extension of the clot to the pontile vessels. This was based on the diagnosis of ninth, eleventh and twelfth nuclear paralysis, associated with paralysis at the decussation of the pyramids. The examination of Dr. Shannon, which disclosed that the eyeball would rotate freely to the right, above and below, but would not rotate to the left, was interpreted to indicate a lesion of the sixth nerve or the vestibular nucleus of the eighth nerve. In addition to these nuclear disturbances, the patient had a left facial palsy.

The presence of normal cerebrospinal fluid, the absence of vascular syphilis and the failure to obtain a history of a toxic vascular disorder due to tobacco or alcohol led us to infer that we were dealing with angiospastic anemia localized in the upper part of the spinal cord, medulla and pons. This belief was fortified by the absence of any other vascular lesion observable post mortem and by the symptom complex beginning when this patient was 18 years of age and terminating with death six years afterward by local vascular thrombosis. We believed that

we were dealing with angiospastic anemia, the counterpart of Raynaud's disease observed in the extremities. All of us in general surgery have seen gangrene of the toes which was preceded by ischemia and cyanosis. Possibly closer observation of these vasospastic disorders of the brain may throw new light on what is now considered hysteria, by interpreting some of the symptoms observed in this disorder as being due to anemia of the vital centers, the result of vasospastic ischemia.

CAUSALGIA OF THE ULNAR NERVE WITHOUT MOTOR AND OBJECTIVE SENSORY DISTURBANCES. DR. ALFRED GORDON.

A woman, aged 40, without a history of trauma or other evident etiologic factors, had burning and lancinating pain in the distribution of the right ulnar nerve at the wrist and hand two years prior to presentation. The burning sensation appeared in paroxysms many times a day, especially on being touched or by movement of the hand. During the attacks there were vasomotor disturbances, namely, redness and elevation of temperature in the hand, as well as perspiration. At other times the hand became cold, pale and dry. The thenar and hypothenar areas were diminished in size. Pressure on the main nerve trunk or at the wrist and hand provoked no pain. Sensation was intact.

About a year before presentation the same sensation developed over the ulnar nerve at the elbow and higher up. The case seemed to be typical of those described by Weir-Mitchell with regard to intensity, duration and resistance to ordinary therapy. In the majority of cases of this kind there is a history of trauma. The symptoms were apparently not those of ordinary neuritis, but rather a result of an abnormal hyperexcitability of the sympathetic centers, stimulation of which provoked in a centrifugal manner a series of vasomotor and secretory disturbances. The condition may result from hyperexcitability of the peripheral sympathetic fibers accompanying the main nerve trunks or the blood vessels. Some cases have been observed of the association of causalgia and neuritis in which section of the nerves relieved the neuritic symptoms but left the causalgia unimproved.

DISCUSSION

DR. J. C. YASKIN: Is there some way of accounting for the difference in the width of the palpebral fissures in this case? How does this patient get relief? Does she obtain relief from hot or cold applications?

DR. ALFRED GORDON: I forgot to mention that examinations of the blood were made, with negative results. The smallness of one palpebral fissure dates from childhood. It is striking, but has no relation to the present condition. Roentgenographic examination for a cervical rib was negative. When the patient has the attacks, she feels a slight relief with hot applications, but this cannot be used as a continuous therapeutic measure. Medication has given no relief whatever.

KLIPPEL-FEIL SYNDROME: REPORT OF A CASE. DR. ROBERT MATHEWS.

In an article entitled "Absence of the Cervical Spine" (*J. A. M. A.* **98**:129 [Jan. 9] 1932) Bauman described a rare form of cervical anomaly known as the Klippel-Feil syndrome, first described in detail in 1912, although it had been recognized previously. According to Bauman, about thirty cases were recorded in the literature prior to the report of his series, which consists of six cases. There may, however, be a number of such cases recorded under a variety of other titles, since the deformity is frequently associated with other anomalies of the skeleton and with various neurologic conditions. A case of congenital elevation of the scapula (Sprengel's deformity) with a defect of the cervical spine (Klippel-Feil syndrome) associated with syringomyelia was reported by F. S. du Toit (*Brain* **54**:421 [Dec.] 1931), who mentioned a somewhat similar case reported by Critchley and MacDonald in 1926. Neither of these cases is referred to in Bauman's bibliography.

The condition is characterized anatomically by the absence, deformity or fusion of certain of the cervical and thoracic vertebrae and at times by the

presence of spina bifida occulta in that area. Clinically, the patients exhibit a rather typical deformity. The neck is short; in fact, it may appear to be absent. There is a low hair line. The trapezius muscles are spread out and may extend almost to the shoulder tips, and there is a limitation of motion in all directions. In Bauman's series, four of the patients were unable to dissociate the movements of the hands, and these so-called mirror movements were reported to be present in an aunt and cousin of one of the patients, although these relatives had no observable spinal anomalies.

The etiology is obscure, but all the changes apparently occur during intrauterine life. A rather high percentage of the patients are mentally defective.

Torticollis is usually present but not marked, and tonic spasm of the cervical muscles is common. It is thought that the muscular system aids the bony structures in supporting the head. Difficulties in breathing and swallowing are sometimes encountered. Facial asymmetry and extra-ocular palsies are described in a certain percentage of cases. The condition is at times mistaken for tuberculous spondylitis, since it is difficult to obtain satisfactory roentgenograms.

Case Report.—E. S. is a mentally defective boy whose chronological age is 13 years; the mental age is 6 years and 10 months, with an intelligence quotient of 59. So far as is known, the family history is negative for deformities. The child was born at full term, and birth was normal. Immediately following birth it was noted that the child was not normal; he appeared weak and was unable to nurse at the breast. Very early in life he was placed in a home for infants. He began to walk and talk at about 2 years. At 3 he was returned to the care of his mother. There is an indefinite history of convulsive seizures while in the home for infants. When returned to his mother's home he showed increased psychomotor activity and a definite behavior disorder. He was difficult to control, stubborn and disobedient. When he reached school age he was enrolled in the public schools, but was sent home because of nonconformity. At the age of 7 he became so difficult to manage that placement became advisable, and he was committed by court order to the Philadelphia Institution for Feeble-Minded. He has adjusted well to institutional life and has shown some response to training and education. He has first grade academic ability. There has been definite improvement in behavior during the past several years. He is now cooperative and obedient. However, there has been a slight drop in the mental level.

He is somewhat undernourished and underdeveloped. The head is slightly small in proportion to the size of the body and is not symmetrically developed. There are a prominence in the left temporoparietal region and flattening on the opposite side of the head. The face is asymmetrical, the left side being more prominent. The nose is short and the bridge flattened and widened. The eyes are normal except for a slight muscular imbalance and a slight internal strabismus. There is a suggestion of epicanthus produced by the widened bridge of the nose. The pupils are round and equal and react promptly to light and in accommodation. The teeth are in fair condition. The tongue protrudes in the midline without tremor. The tonsils are somewhat enlarged. The neck is deformed, and this is the most outstanding feature of the physical examination. It is broad and short. The hair line reaches almost to the shoulders. The trapezius muscle stands out prominently on either side, but is most marked on the left. There is limitation of motion of the head in all directions, but it is possible for the patient to rotate the chin slightly more to the left than to the right. The deformity produces an appearance suggesting that the child is resting the chin on his chest at all times. There is a slight bilateral torticollis. The posterior cervical group of muscles remain in a state of spasm and are quite tense. They probably aid in the support of the head. The scapulae are high, producing a condition described as Sprengel's deformity. The thorax is fairly well developed; the expansion is limited but equal. The heart, lungs and abdomen are normal. The external genitalia are underdeveloped. The extremities are well developed, and there are no deformities.

The motor defects resulting from the deformity of the cervical spine have already been noted. The deep and superficial reflexes are present and active

throughout. Tapping the biceps tendon produces a flexion of the thumb and index finger of either hand. This is more marked on the right. There are no pathologic reflexes. Station is normal, but gait is slightly awkward. There is no dysmetria or muscular incoordination. There are no sensory changes.

Roentgen examination revealed an absence of certain of the cervical vertebrae and a deformity and fusion of the remaining vertebrae. There was a spina bifida occulta in the cervical and upper thoracic regions. Individual vertebrae of the cervical group could not be identified.

LABYRINTH AND CORTEX (THE ELECTRENCEPHALOGRAM IN THE STIMULATION OF THE LABYRINTH). DR. E. A. SPIEGEL.

This article will be published in full in a later issue of the ARCHIVES.

NERVOUS SYMPTOMS IN POSTHEMORRHAGIC SECONDARY ANEMIA. DR. SAMUEL B. HADDEN.

In 1878 the pathologic picture of posterolateral sclerosis was described by Kahler and Pick, and in 1887 Lichtheim pointed out the frequency of the relationship of this neurologic condition to pernicious anemia. At the present time the symptom complex of posterolateral sclerosis is regarded as almost exclusively the result of primary pernicious anemia. The relationship of secondary anemias to changes in the nervous system is less well known. Changes in the cord occurring in secondary anemia have been reported, but not all these cases can be accepted as authentic.

Oppenheim believed that in all cases of posterolateral sclerosis the anemia need not be pernicious and reported one case in which the posterolateral sclerosis was the result of cachexia due to a malignant tumor, another instance occurring during the anemia of lactation and three instances occurring in persons in the sixth and seventh decades of life who had anemia attributed to chronic malaria contracted in early life. These cases were reported before present knowledge of pernicious anemia and cannot be accepted unequivocally as due to secondary anemia.

Sargent reported cases of simple achlorhydric anemia in which symptoms of posterolateral sclerosis existed and in which marked improvement in both the blood picture and the nervous symptoms occurred from iron but not from liver therapy. This worker believed that in all types of anemia, including the pernicious type, the nervous symptoms are more promptly and effectively improved by massive doses of iron than by liver therapy alone. All of his patients received 150 grains (9.75 Gm.), or more, of iron each day.

The view that the anemia is not the main factor in posterolateral sclerosis of the primary pernicious type seems apparent, as many times the nervous symptoms long precede the blood picture of anemia. Castle stated that pernicious anemia is the result of the absence of a specific intrinsic factor of the gastric juices, and frequently nervous changes are noted in other diseases associated with achylia gastrica, notably in pellagra. In tapeworm and hookworm anemias and in the anemia of sprue, symptoms of disorders of the nervous system are encountered, but they may result from the toxic factors of the disease.

In many of the diseases caused by dietary deficiency there is an associated anemia with nervous symptoms, but the work of Mellanby tends to prove that here again the anemia cannot be considered the important factor, as in all his experimental animals he was able to prevent degenerative changes in the nervous system by the addition of vitamin A or carotene to the diet. In all his animals he was able to demonstrate diminution or depletion of the vitamin A content of the liver, and in some cases of posterolateral sclerosis of pernicious anemia he found a decrease in the amount of vitamin A in the liver.

Weil and Davidson in their exhaustive pathologic studies on the spinal cord in anemia concluded that posterolateral sclerosis probably never occurs in any secondary anemia. In their series of cases of secondary anemia, changes in the

cord were noticed in a few in which the differentiation between primary and secondary anemia was not clear. They included in their group of secondary anemia all cases with a concentration of hemoglobin of 75 per cent or less and with 3,500,000 red blood cells or less. In only six of their cases, not including the four with leukemia, was the red blood cell count under 3,000,000, and in only three cases was the hemoglobin under 50 per cent. In one of these cases, involvement of the column of Goll was noted in a patient who died of tuberculous meningitis. The concentration of hemoglobin in this case was 28 per cent. The cases of secondary anemia which showed changes in the central nervous system were usually the result of metastatic or myelitic lesions. In the paper of Weil and Davidson the number of cases of really severe secondary anemia is too few to warrant their conclusions that changes do not occur in the cord in this condition.

The cases of anemia with symptoms of the central nervous system which I present in this paper are very severe; there was rapid diminution of the hemoglobin and red blood cells to almost fatal levels by massive hemorrhage from medical causes.

CASE 1.—A report of this case was presented before this society a few months ago by Dr. A. Tornay from my service at the Episcopal Hospital. Briefly, the patient, a woman, aged 40, suffered from severe postpartum hemorrhage on March 1, 1927. She was in a stuporous state for several days following delivery, and complained of blindness and a cold numb feeling of the body, especially in the lower extremities. It was several weeks before vision returned to what she considered normal. On getting out of bed she experienced considerable difficulty in walking because she could not tell the position in which she placed her feet and had to watch the ground constantly. The patient states, and her friends confirm the statement, that the hemorrhage was so severe that coal shovels and buckets were used to scoop up the clots after delivery. There can be no question that the hemorrhage was unusually severe. When she was observed at the Episcopal Hospital during November and December, 1932, there were a suggestion of nystagmus, incoordination in the finger-to-nose test, marked symptoms in the pyramidal tract and the posterior column, diminution of visual acuity, with evidence of old optic atrophy, concentric concentration of the visual fields and normal gastric contents and blood picture. The colloidal gold test showed an alteration in the first zone.

CASE 2.—This case was reported clinically before this society by Dr. W. L. McConnell in January, 1907, and is included through the courtesy of Dr. William G. Spiller. The patient was admitted to the hospital in December, 1903, and died in October, 1924. A few days before admission, the patient, while a prisoner in the county prison, had a massive gastric or pulmonary hemorrhage. The following day he noticed dimness of vision. Sight gradually failed until, one week after the hemorrhage, vision was lost in both eyes. Shortly after the hemorrhage he experienced weakness in both legs and eventually entirely lost his ability to walk. Power in the legs, however, was never entirely lost. Three months after the weakness in the legs set in he began to experience weakness in both upper extremities. Improvement was gradual; approximately ten months later he was able to stand and walk a little, although he was extremely ataxic. Examination by Dr. Spiller in August, 1904, showed wasting of the upper limbs with intact sensation, and marked weakness and wasting of the lower extremities, marked diminution of the left and loss of the right patellar reflex, and a bilateral Babinski sign.

The patient improved gradually and eventually was able to walk without great difficulty. He had for a long time decided bilateral toe drop. His reflexes were variable. At times they were exaggerated. He never regained vision. He died of a stroke in 1924.

At the time of admission, the first blood count revealed: hemoglobin, 16 per cent, and 1,175,000 red blood cells. The condition remained grave for some time, but gradually improved. Loss of vision was permanent. For many years signs of involvement of the pyramidal tract persisted.

Pathologically, the brain presented multiple areas of softening, with advanced arteriosclerosis, and in the cord mild bilateral degeneration of the pyramidal tract was noted. This diagnosis was confirmed microscopically. Degeneration of the optic nerves was advanced.

It is unfortunate that cerebral softening complicated this case, since this vitiates the pathologic findings, but there is little doubt that the symptoms followed severe posthemorrhagic anemia.

Case 3.—E. B., aged 39, was admitted to the Presbyterian Hospital in March, 1932, and discharged in June, 1932. The patient had been having prolonged menstrual periods with profuse bleeding for two years, each period lasting from three to fourteen days and always being excessive. Fifteen days prior to admission she had profuse bleeding, with actual gushing at times. She was confined to bed for four days prior to admission because of weakness, and during this time large vaginal clots were passed. At the time of admission she was extremely weak. The skin and mucous membranes were definitely blanched. The blood pressure was 100 systolic and 44 diastolic. Vaginal examination revealed a soft cervix, four fingers dilated, through which a soft round mass was being expelled. A tentative diagnosis of incomplete abortion was made. The hemoglobin on admission was 45 per cent; the red blood cells numbered 1,880,000, the leukocytes, 22,000.

The patient began to bleed profusely at midnight of the day of admission. The following morning she was given 300 cc. of citrated blood and 2,500 cc. of saline solution. On March 15 an attempt was made to evacuate the uterus, but the bleeding was so profuse that the attempt was stopped. In the next few days she became extremely drowsy and confused, and was aroused only with some difficulty; four days after admission she became definitely blind and had little more than perception of light. Three blood transfusions were made. My examination revealed a confused, blind woman, who had a definite increase of muscular rigidity, with some twitching movements, especially in the lower extremities. The reflexes were all extremely hyperactive. Two days later she was able to see objects moving in front of her eyes, but not distinctly. At this examination there appeared to be evidence of contraction of the visual field. The pupils reacted very slowly to light. There was no visual paralysis noted. The reflexes were still definitely exaggerated. The plantar reflexes were indefinite. There was a suggestion of ankle clonus on both sides. The twitching movements previously noted were largely confined to the lower extremities and were irregular. The expression was fixed. There was considerable rigidity, with a suggestion of catatonia, and some limitation of upward associated ocular movements was noted. Vision improved slowly but steadily, so that central vision tested with a card was one tenth of normal. Hysterectomy and appendectomy were performed later, and the patient was found to have an adenomyoma of the cervix of the uterus. At the time of discharge from the hospital, vision was normal in the left eye, with one-half vision in the right eye. The nerve heads were very pale, and the visual fields were concentrically contracted.

This case is of interest because recovery from severe symptoms was apparently almost complete. Three days after admission to the hospital the hemoglobin content had dropped to 27 per cent, with 1,200,000 red blood cells. After that, as a result of transfusions of 2,000 cc. of blood, the patient improved rapidly and the severe symptoms disappeared. Only the prompt restoration of the blood by transfusion enabled this patient to survive. At the present time Dr. Langdon reports her corrected vision as normal, but the visual fields are contracted. No neurologic examination has been made.

Comment.—In all three cases, disturbance of vision was profound early in the course of the illness. Reports of transient and permanent blindness are not uncommon following hemorrhage. Hayes, in Norris and Olive's "System of Diseases of the Eye," reported eleven cases of blindness following hemorrhage, ten after gastric hemorrhage and one after hemorrhoidal bleeding. Larrey, in his medical memoirs of the Napoleonic campaigns, did not mention a single case of this sort, and the post-World War literature does not reveal similar cases,

although massive hemorrhage was common. Soldiers are usually in excellent health, and recovery from surgical hemorrhage is usually prompt.

Conclusions.—1. The system complex of posterolateral sclerosis is usually the result of pernicious anemia. 2. Secondary anemia, especially posthemorrhagic, produces profound changes in the central nervous system, not consistently characteristic, but degeneration of the optic nerve and pyramidal tracts seems to occur most commonly. 3. Prompt and adequate transfusion tends to prevent the permanence of these serious symptoms.

DISCUSSION

DR. H. M. LANGDON: Loss of vision from severe anemia following massive hemorrhage is rather uncommon; as Dr. Hadden has said, it practically never occurs in hemorrhage from other than medical causes. He has cited two wars in which this condition was studied. During the Franco-Prussian war, von Graefe and some of his colleagues searched for this condition but did not find a single case. It has never been reported after hemorrhage from trauma, but only after hemorrhage from disease conditions; it has always been believed that some factor other than the mere anemia was involved in the loss of vision. Once the vision is lost or once the loss of vision is started it usually progresses to complete blindness, which is possibly of central origin, though Ward Holden believed that it was retinal, having found degeneration of the ganglion cell layer of the retina. The patient in case 3, whom I saw at the Presbyterian Hospital, was, I believe, fortunate in having prompt massive transfusions of blood, as otherwise I think the sight would probably have been lost.

I think that this is the first case on record in which massive transfusions have been used in this condition. The result was gratifying, and the woman now has a central vision which is normal, and shows a field cut to about 20 degrees on the perimeter. I think, however, that it is really somewhat better than this. She is pessimistic and insists that she cannot read and cannot see. Her husband thinks that a mental depressive state is responsible for this complaint, and I feel sure that the field of vision is better than she will admit. The prompt return of vision in this case, after the transfusions of blood, with no other factor in the condition being altered, makes it seem possible that in spite of preconceived notions the anemia is the sole factor in the loss of vision.

DR. S. F. GILPIN: The third patient, Mrs. B., has been under my care since her discharge from the Presbyterian hospital. She showed no evidence of organic disease of the nervous system as to reflexes, pupillary reaction, sensation, sphincteric control or station. She presented a fine tremor of the lips, tongue and fingers. She showed some muscular rigidity on sitting or rising from a chair. She was somewhat rigid in walking and had a tendency to carry her arms at her sides in an immobile position. Her face lacked expression, and her speech was a monotone. For several months I feared that the paralysis agitans syndrome was developing, and I cannot as yet feel positive that she will escape it. At present all the symptoms have greatly improved, so that she walks, gets up from her chair and sits down again with very slight rigidity. She still has a staring expression. Her mental action is good, and she now takes an interest in her home. In the beginning she was slow mentally, though her memory was good. She still complains that she cannot see, though she can read the finest print.

DR. N. W. WINKELMAN: I have been on the lookout for cases with a pathologic process in the spinal cord with hemorrhage. I have never been able to satisfy myself in any case that hemorrhage is capable of producing a degeneration of the spinal cord resembling that in pernicious anemia. It must be realized that a pathologic process in the spinal cord can be advanced in cases of pernicious anemia with a normal blood count, as in one case reported in which the process was extreme as seen under the microscope and yet the blood picture for days before death showed a comparatively normal count. It is therefore not the anemia per se that produces the degeneration of the cord. In no case of pernicious anemia, no matter how severe, has degeneration of the cord been uncovered.

In cases of sudden loss of blood, as, for example, post mortem, or in bleeding from a gastric ulcer, the changes in the central nervous system that we have been able to uncover have been exactly like those due to anoxemia from any cause. These changes have not been limited to the spinal cord but have been universal in the central nervous system. The changes resemble in many ways those from anemia the result of carbon monoxide poisoning. Dr. Gilpin's description of one of Dr. Hadden's cases, months after the hemorrhage, fits in with a change in the pallidum, such as is frequently found as an after-result of carbon monoxide poisoning. In several cases in which anoxemia has been the result of cessation in breathing during operative procedures the changes in the central nervous system have been strikingly similar to those in severe hemorrhage.

It thus becomes obvious that when hemorrhage is sudden, the changes in the central nervous system are the result of anoxemia. When the anemia is of the secondary type and is slowly progressive, there are usually no changes in the spinal cord which could in any way be mistaken for those in pernicious anemia.

Book Reviews

Nervous Breakdown: Its Cause and Cure. By W. Béran Wolfe, M.D. Price, $2.50. Pp. 240. New York: Farrar & Rinehart, 1933.

As it is written for the nonmedical public, "Nervous Breakdown" will undoubtedly be presented by perplexed patients to psychiatrists with the query: "Will this book help me?" The question merits serious consideration and deserves a thoughtful answer, for the always suggestible neurotic person cannot recklessly be exposed to every volume of popular psychology advertised by the publisher. The fluent, almost flippant style in which Wolfe writes will charm some readers; many nervous patients, however, will be discouraged by this jovial presentation, feeling perhaps that they are not being taken seriously. Intelligent readers may be disappointed by the narrowness of the author's point of view, notably by his failure even to mention any explanation of the neurosis other than the Adlerian one.

A melodramatic pose pervades the book from its dedication ("To men and women in perplexity") to its final sentence ("I give you courage, hope, and the will to get well!"). The rashness which prompts Wolfe to use the word "cure" in his subtitle, and which is further evidenced by such phrases as "Your symptoms will disappear as if by magic," will win no friends among the medical profession. Nor does the author's offer of his services as a director of the depressed reader's personal suicide club, or his suggestion that the patient write him a letter about his symptoms, suggest the scientific disinterestedness that is essential in a volume of this type.

Dr. Wolfe is skilful in coining happy phrases, a tendency which is unfortunately tainted by his childish pride in his own creations. His ingenious expressions, "self-sabotage," " a belligerent *it* ," "sexual athletics" or "lying the truth" would have been more effective without the "as I have called it" preceding or following. In spite of his repertoire of original phrases, the author finds it necessary to pad the book with clichés; within the first thirty pages such venerable wheel horses as "Nature in her infinite wisdom," "the game is not worth the candle," "all their eggs in one basket" and "wins half the battle" are found. The plethora of stereotyped phrases is matched by the presence of numerous unsubstantial generalities of the order of "service to my fellow man," "cultivate creative self realization," "live dangerously," "live in the present" and "courage, cooperativeness, and spiritual independence." The critical reader will wish that Dr. Wolfe had used a dictionary of symptoms; at least the battology of "exquisitely" ("exquisitely designed" and "exquisitely germaine" within seven pages and "exquisitely appropriate" in a subsequent chapter) might have been avoided.

The book is divided into seven chapters; all but one are captioned in the grand style of the eighteenth century: "Of Causes," "Of Symptoms," "Of Cases and Cures." After three chapters bearing the latter title, the reader suddenly comes to chapter 6, "Plain Words to Patients." The book closes with a chapter bearing the designation "Of Creative Self Realization." Chapter 1 promises but fails to define a nervous breakdown; a simile ("A nervous breakdown is a personality knock-out") replaces a definition. The mechanism, Wolfe believes, is always that of flight from an intolerable situation. This he terms a "face-saving device." The neurologist who reads chapter 2 will be unable to know if the syndrome under discussion is a manic-depressive or a psychoneurotic attack. Little help in understanding the author's conception is offered by his formulation of a "Decalogue of the Nervous Breakdown." In the next three chapters, nine case reports are given, illustrating instances of adolescent breakdown, social breakdown, sexual ignorance, masturbation, masculine protest, romantic illusion, homosexual difficulty, economic collapse and family breakdown. The cases are well selected, the mechanisms clearly explained, the recoveries logically developed. To patients whose

neurosis can be fitted into one of these categories, this section of the book should offer a hopeful outlook.

Chapter 6 ("Plain Words to Patients") is the climax of the book; it is to these pages that worried patients will turn first. The intelligent reader will be repelled by its gushing and saccharine unctuousness, for he is told to sit in his favorite chair, light his pipe, choose a phonograph record and play the music softly. The author modestly announces that he is "only a doctor who has devoted his life to the healing of the mentally ill," adding, "I have discovered some truths and some technics that have proven valuable in the treatment of cases like yours." After a review of the mechanism of the breakdown, another decalog is offered. This is composed of ten items to be memorized, catechism fashion, and to be reread or recited twice a day. The first commandment is: "I have a nervous breakdown. This means I have been swimming against the current of life, not with it. Nature has warned me. . . . I am going to take Nature's warning. I cannot personally upset the laws of Nature . . . 50 billion years of evolution can't be wrong." Other items include: "My symptoms will disappear when I find a better way of living," and "I will not talk about my symptoms," reaching a final triumph of jejune generality in ". . . the only real satisfaction of life consists in an ideal of 'face' based on service to my fellow man."

The final chapter consists of advice on how to get along with oneself, how to use one's leisure time, how to cultivate a sense of humor, how to live in the present and how to become emotionally mature.

In the middle of chapter 5, Wolfe makes an excursion into economic theory, presenting a dissertation on the depression covering more than sixteen pages. It is difficult to see what place such a treatise has in this volume, except to impress the reader with the author's cultural breadth or to illustrate the range of his cleverness. If this is Dr. Wolfe's intention, the excursion was quite necessary.

The book suffers from occasional and glaring inconsistencies. The advice to be colorful and vigorous may be contrasted with the advice to avoid arguments; the insistence on abandoning romantic illusions is grossly at variance with the sermon on living dangerously. There is a mystical footnote on telepathy (about "two vital rhythms which are closely contrapuntal") which is out of place in a book nominally devoted to sanity, logic and the scientific method.

"Nervous Breakdown" has several good features: It removes the stigma from the neurosis; it offers hope to the unhappy patient; it presents a variety of cases, which readers will refer to themselves, in which recovery had occurred; it cites practical suggestions for every-day behavior.

But when the balance is struck, the book will be found on the debit side. In some respects it frightens the patient. For example, the author sensationally warns that recovery from a breakdown without outside assistance predisposes to another attack. "In such cases," Wolfe says, "no true cure is effected . . . he has simply laid himself open to future difficulties. . . . Nothing could be more futile than the false pride of the patient who has had a nervous breakdown." The author has probably failed to realize the seriousness of these lines. This paragraph will haunt every recently recovered neurotic person who reads them, reawakening forgotten fears. Equally unfortunate is Wolfe's hysterical condemnation of the romantic illusion. He states that the person who believes that adultery is a sin, that children should obey their parents implicitly or that love is a prerequisite to happy marriage is an infantile romanticist whose beliefs "may sooner or later involve him in a critical situation in which he will be compelled to save his face by having a nervous breakdown." While it is true that these ideas are unintelligent, it is likewise true that most people hold them. The effects of such a pronouncement on the nervous reader can be but to add one more burden.

Particularly dangerous is the implication that this book should be used as a therapeutic manual before seeking psychiatric advice. One of the last statements —and one, therefore, most likely to linger—is: "If you have carried out the instructions in this book and no relief is obtained, I counsel you to put yourself in the care of a reputable psychiatrist." The patient will inevitably understand

the implication that earlier medical consultation is unnecessary. The possibility of organic disease being self-diagnosed as neurotic with the resultant loss of time from essential treatment, while the patient is seeking a cure by Wolfe's advisements, should have been obvious to the author.

"Nervous Breakdown" is badly written, water-logged with stereoptyped phrases, padded with loose generalities and weakened by inconsistencies. It strives for cheerfulness and attains flippancy. Its claims are rash, its point of view narrow. Both in its phraseology and in its thoughts it is tiresomely repetitive. It is crudely self-glorifying and utterly without dignity. It gives the distressed reader the impression that he is not being taken seriously. It is as sensational as a radio health talk. It encourages self-diagnosis and self-treatment in a field in which this is particularly dangerous. It will appeal to the gullible members of the lay public.

The Nature of Human Conflicts: Or Emotion, Conflict and Will. An Objective Study of Disorganization and Control of Human Behavior. By A. R. Luria, Professor of Psychology, State Institute of Experimental Psychology, Moscow, U. S. S. R. Translated from the Russian and edited by W. Horsley Gantt, Phipps Psychiatric Clinic, Johns Hopkins University. Price, $4. Pp. 428, with 133 illustrations. New York: Horace Liveright, Inc., 1932.

Interesting studies are frequently appearing from Soviet Russia, and this large book is not the least interesting of present Russian scientific studies. It consists largely of accounts of laboratory experiments performed on human beings to ascertain the origin of mechanisms which may be the basis of "the disorganization of human behavior," and further elaborates in detailed, involved discussion the results of these experiments to see if any approach to proper conceptions of regulation of behavior might be found. The work is done by a leading Russian psychologist and is made available to English readers by Dr. Gantt, of the Phipps Psychiatric Clinic, who has spent many years of study in Russian scientific circles.

The experiments are typical of those found in any first-class psychologic laboratory, but are somewhat unique in that a varied number and kind of subjects were used, including criminals, children and definitely neurotic persons, as well as university students as normal persons. The studies cover the motor responses, on kymographic records, of the right and the left hand and speech response, and include descriptive studies of general behavior of the subject. A "functional barrier" is found to exist within the active function of the nervous system, and it stands between the original excitation and its outlet in the motor sphere. It is altered under different conditions, according to the immediate needs of the organism. Mental conflict and affect are shown in the experimental results to change or destroy this "functional barrier," and the presence of neurosis is explained on the basis of the destruction of this barrier. The barrier does not exist in childhood; it is "not a natural mechanism but one of cultural origin," a functional inclusion in the organism.

The conclusions are far too extreme and the discussion is much too involved, whether it is because of the original text or because it is a translation. Nevertheless, the approach of the work as a whole is unique and will give interesting reading to every one working in psychiatric and psychologic fields, for the book as a whole is a good attempt at correlation between functional and organic fields.

A Critique of Sublimation in Males: A Study of Forty Superior Single Men. By W. S. Taylor. Genetic Psychology Monographs, January, 1933. Volume XIII. Number I. Paper. Price, $2. Pp. 115. Worcester, Mass.: Clark University Press, 1933.

This study is one of a series of monthly monographs, all dealing more or less with psychologic subjects. Several years ago the author submitted a questionnaire to forty superior single men to ascertain in detail what sexual adjustment they

were making. The purpose was to determine how much actual sublimation entered into their adjustment, as the author questioned the theoretical and practical validity of the psychoanalytic conception of sublimation and also wished to contribute something toward a better understanding of masculine sexuality. After ten years, a thorough check-up was made, and further corrections and additions were secured from the subjects submitting the questionnaires.

The study as a whole is a typical compilation of results as secured from the questionnaire type of study. The discussion the author presents on his findings is interesting. He did not find a single man who pretended to sublimate completely; he is convinced that all answers were given frankly and that there was no particular evasion. He states: "There is in young men an irreducible minimum of sexuality . . . never transmuted or sublimated away. On the contrary, it requires and finds some direct outlet in every case."

In the last chapter he discusses the relation of his findings to social and ethical problems. There are no final conclusions given, but the point of view presented indicates the belief of the author that some type of sublimation should be achieved even if he has found it not to be truly present (in the psychoanalytic sense) in the results of his study. There is little in the results obtained by the questionnaire method that cannot be found in the daily experience of every active clinical psychiatrist. The author appears to have minimized the importance of unconscious processes as regards the sexual life.

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